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FDA wants to hear from you: Proposed framework for regulating output of digital health tools accompanying prescription drugs as labeling

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On November 20, the Food and Drug Administration (FDA) published a request for comments on a proposed framework for regulating the output of digital health applications disseminated by or on behalf of drug manufacturers with one or more of their prescription drugs. FDA Commissioner Scott Gottlieb, M.D. touted the proposed framework in his remarks at the Reagan-Udall Foundation on November 19: "We believe the flexible concepts we've put forward will encourage more drug sponsors to advance beneficial and innovative software apps with FDA-approved drugs and biologics."

In issuing this request for comment, the FDA signaled its intention to develop guidance on this topic, but clarified that this notice is not a guidance document itself, but rather is intended to generate discussion. Accordingly, the agency posed a series of questions (noted below) for stakeholders' input. We encourage interested parties to submit comments to this docket to help inform and shape the FDA's views in this developing area.

New terminology: "Prescription drug-use-related software"

In this request for comment, the FDA introduces a new term, "prescription drug-use-related software," (PDS) and defines it as software disseminated by or on behalf of a drug sponsor that accompanies one or more of the sponsor's prescription drugs. Examples of PDS described in the notice include

- software branded with a drug name that a sponsor intends for patients to use to record and track their use of the sponsor's drug with a mobile app, such as an app for patients to record their degree of physical functioning while taking a drug;
- software designed by a drug sponsor for its specific drug that enables a health care provider to enter dosing instructions for a sponsor's prescription drug product that the patient can retrieve through the software; and
- software designed by a drug sponsor to communicate with a device in drug-device combination product regulated primarily as a drug.

The proposed regulatory framework described in this notice relates to the output of the PDS that is presented to the end user, e.g., a patient, caregiver, or health care professional. This output could include screen displays generated by the software, as well as sounds or audio messages. Examples of PDS output described in the notice include

- software that a sponsor disseminates to patients to record and track their prescription drug use with an app, the PDS output would include the screen display where patients record their ingestion of the drug and can view ingestion records over time;
- branded software that provides a risk calculator to assist health care providers in deciding when to prescribe a medication and how to calculate the appropriate dose, the PDS output would include the screen display of the risk calculator; or
- an app that a sponsor disseminates to patients to communicate information from an embedded device that tracks drug ingestion, the PDS output would include screen displays that show the information on drug ingestion, and if the app provides alerts (e.g., that a dose has been ingested) or reminders (e.g., reminding patients to take their medication), these messages also would be considered PDS output.

Proposed regulatory framework for PDS output

In its proposed regulatory framework, the FDA contemplates that the output of PDS could be incorporated in FDA-required labeling or in promotional labeling. PDS output could be incorporated in FDA-required labeling if

- the drug sponsor demonstrates there is substantial evidence of an effect on a clinically meaningful outcome as a result of the use of the PDS with a drug; or
- the software is key to one or more of the intended uses of a drug-led drug-device combination product.

Where the PDS output is not incorporated in FDA-required labeling, the FDA proposes to regulate the PDS output as promotional labeling. As such, this PDS output would be subject to FDA's existing regulatory requirement for submission of promotional labeling materials at time of first use under Form FDA 2253 and would not require FDA review prior to dissemination. The proposed submissions under Form FDA 2253 would include "screenshots or other appropriate representations of what the user will experience."

The FDA notes that under certain circumstances, it may be advisable for sponsors to utilize the voluntary advisory comment process prior to disseminating PDS output that would be considered promotional labeling — in particular, if there is uncertainty about whether the PDS output would be consistent with the accompanying drug's FDA-required labeling. The notice provides examples of situations where seeking advisory comments may be appropriate, such as PDS output that instructs patients on when to adjust their dose based on symptoms without first consulting a health care provider (e.g., an app that allows patients to calculate an insulin dose based on published treatment guidelines and recommends a dose different than that prescribed by the patient's physician).

The FDA acknowledges that software reliability is critical to producing the intended and expected PDS output, however, the agency proposes to assume the drug sponsor will be responsible for assuring the reliability of the software and does not intend for this proposed regulatory framework to reach the underlying software code.

Framework for regulation of digital health tools as medical devices unaffected

Importantly, the regulatory framework for PDS output proposed in this request for comment does not alter the FDA's established regulatory framework for medical devices. This framework would not change the analysis of whether the PDS itself meets the definition of a medical device or falls within the FDA enforcement discretion policy related to software as a device, or whether the PDS and drug together meet the definition of a "combination product." PDS that separately meet the criteria for regulation as medical devices — either on their own or as part of a drug-led combination product — would still be subject to those requirements, as well as the promotional labeling oversight proposed in this request for comment.

The proposed regulatory framework also does not apply to software developed by third parties who develop and disseminate software for use with a prescription drug independent of the drug sponsor. These third party developers would be subject to the FDA's existing regulatory framework for software as a medical device and would not be subject to the labeling oversight proposed in this request for comment.

This proposed framework builds on the FDA's trend toward providing clarification and guidance related to digital technologies, as evidenced by

- the FDA's digital health software precertification program ("Pre-Cert," analyzed here, here, here, and here);
- the FDA's April 2018 Medical Device Safety Action Plan and other guidance documents that highlight the agency's heightened focus on cybersecurity (analyzed here);
- the FDA's April 2018 draft guidance on Multiple Function Device Products (analyzed here);
- the FDA's July 2017 Digital Health Innovation Action Plan (analyzed here); and
- other guidance documents (analyzed here) that aim to clarify the framework for the regulation of software and digital health products to bring FDA regulatory policy into line with the 21st Century Cures Act.

Request for comments on the proposed framework for PDS output

The FDA specifically requested comments on several questions, including whether the proposed framework for PDS output

- would adequately foster innovation by drug sponsors;
- considers the appropriate factors in applying prescription drug labeling requirements to PDS output;
- appropriately characterizes the types of PDS output that should be submitted for advisory comment;
- adequately assures patient safety by assuming sponsors will be responsible for ensuring that PDS reliably produces its output as intended;
- provides sufficient oversight of software updates; and
- facilitates timely generic competition for prescription drugs that are approved with PDS output in their FDA-required labeling.

The FDA also requested input on alternative regulatory approaches it should consider for PDS output and what considerations it should apply in developing recommendations for presenting a fair balance of benefit and risk information in PDS output.

The docket for this request for comments will be open until January 22, 2019. If you have any questions on this proposed regulatory framework or wish to comment, please contact any of the authors listed below or the Hogan Lovells lawyer with whom you regularly work.

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