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# FDA Issues Draft Guidance Regarding Waiver of Single Shared System REMS Requirement

FDA Commissioner Scott Gottlieb has vowed to take steps to speed the review and approval of generic drugs as part of his overall priority to address concerns about drug prices. While FDA has very limited authority regarding drug pricing, Commissioner Gottlieb has pushed to encourage generic competition and has sought to address regulatory issues that he believes could be impediments to that competition. To that end, Commissioner Gottlieb has cited the statutory provision requiring a single, shared system ("SSS") for a risk evaluation and mitigation strategy ("REMS") with elements to ensure safe use ("ETASU") as a potential obstacle in the way of generic drug approval. Pending legislation, discussed more fully below, may clarify FDA's ability to move away from the statutory preference for the SSS REMS. In the meantime, however, on May 31, 2018, FDA issued draft guidance regarding the waiver of the SSS REMS requirement that (1) largely replicates what is already in the statute; (2) sets forth the agency's current standards and processes for assessing a waiver application; and (3) implies that FDA may be interested in granting more waivers going forward.

## Statutory Background

Section 505-1 of the Federal Food, Drug, and Cosmetic Act ("FD&C Act") authorizes FDA to require a REMS if FDA determines that a REMS is necessary to ensure that the benefits of a drug outweigh its risks. Examples of such REMS include medication guides that provide risk information to patients, communication plans for health care providers, and/or ETASU, when such elements are necessary for risk mitigation. ETASU may include such elements as training for health care providers or monitoring of patients. REMS generally involve a timetable of submission of assessments of the strategy, and may include an ETASU implementation system.

Section 505-1(i)(1)(B) of the FD&C Act requires abbreviated new drug application ("ANDA") applicants referencing a drug with a REMS with ETASU to use an SSS, unless otherwise waived. However, FDA is authorized by statute to grant a waiver of the SSS requirement and permit the ANDA applicant to use a "different, comparable aspect" of the ETASU. Such waivers have been granted by FDA three times. Section 505-1(i)(B) expressly allows for waiver of the SSS requirement in two situations. FDA may grant a waiver if it finds that, pursuant to section 505-1(i)(B)(i), the burden of creating an SSS outweighs the benefits of a single system. FDA may also grant a waiver if, pursuant to section 505-1(i)(B)(ii), an aspect of the ETASU is claimed by an unexpired patent or is a method or process that is entitled to protection as a trade secret, and the ANDA applicant certifies that it sought a license for use of the aspect, but was unable to obtain one.

## Draft Guidance

FDA's draft guidance seeks to clarify the agency's policy on SSS REMS waiver requests, but is limited to waivers of the SSS requirement where there is no previously established SSS and no previously approved separate REMS for ANDA(s) that the application can join.

The draft guidance primarily addresses waivers pursuant to section 505-1(i)(1)(B)(i). According to the draft guidance, in order to determine whether a waiver is appropriate, FDA will compare the benefits of an SSS compared to the burden, taking into account the impact on health care providers, patients, ANDA applicant(s), and the reference listed drug ("RLD") holder. Some of the benefits contemplated by FDA include increased efficiency and

potential for sharing costs between ANDA applicants and RLD holders, as well as shared infrastructure for health care providers. With respect to the burdens involved in forming an SSS, the draft guidance notes that development of an SSS REMS ordinarily involves negotiations and/or agreements between companies that are often competitors and potential adversaries in patent litigation. Additionally, formation of an SSS REMS may be time-consuming and complicated, which may create a delay in access to generic versions of drugs for health care providers and patients.

The draft guidance notes that, while FDA generally notifies an ANDA applicant of a SSS REMS requirement after the ANDA has been received for review, FDA will consider a waiver request at any time. An ANDA applicant may either submit an SSS REMS, or a proposed separate REMS with request for waiver. Regardless of whether the applicant submits an SSS REMS or a proposed separate REMS, FDA will then review the application and recommend that the proposed REMS be submitted to FDA by the midpoint of the pending application review cycle to allow for sufficient time for review. Although a waiver request is not required, FDA encourages the submission of a written waiver request to facilitate its review of the application. The draft guidance instructs ANDA applicants to include a discussion and analysis of the benefits and burdens of having an SSS, as well as a description of the proposed separate program and a description of how aspects of the required ETASU are comparable to those of the RLD REMS. Once a waiver is submitted, FDA will conduct a case-specific analysis for a proposed separate REMS. FDA states that a separate system for ETASU with a waiver of the SSS requirement must include the same ETASU as described in the statute. By detailing the process and standards, the draft guidance appears to provide a roadmap for ANDA applicants seeking to obtain a waiver.

In furtherance of transparency in this area, FDA also issued a second guidance document on May 31, 2018, that describes general principles and recommendations to assist sponsors with developing SSS REMS programs. This draft guidance provides recommendations on the development of an SSS REMS for multiple prescription drug products and discusses benefits of an SSS REMS. FDA outlines situations where it will require or recommend SSS REMS, suggests formation of industry working groups ("IWGs"), and outlines its role in the development of REMS. Notably, FDA does not advise on business arrangements being negotiated, nor arbitrate substantive disputes about terms of contract; instead, its role is limited to setting expectations and "facilitat[ing] collaborations" throughout the process, if necessary. The draft guidance also provides links to resources for industry in preparing REMS submissions, and an outline of timing for REMS applications.

## Pending Legislation

In April 2017, Senator Patrick Leahy introduced the Creating and Restoring Equal Access to Equivalent Samples Act of 2017 ("CREATES Act") that includes provisions to address the SSS REMS requirement and waiver authority. At this time, press reports indicate there are still ongoing negotiations regarding the CREATES Act, but it is unclear if it will be considered or enacted by this Congress. The sponsors of the CREATES Act claim that it is essential for developers of generic drugs to be able to join the RLD manufacturers (also known as "license holders" within the statute) in an SSS of ETASU, and that certain license holders are preventing generic drug developers from doing so through the REMS requirement. Those sponsors assert that antitrust laws are insufficient and that a "more tailored legal pathway" is necessary to ensure competition in the drug and biological products marketplace, and call for "clearer regulatory authority" with respect to the FDA's ability to waive the SSS requirement. In addition to providing a clearer avenue for SSS waivers, the legislative proposal also allows generic drug providers to bring suit against license holders for failure to provide sufficient quantities of a covered product. If the proposals outlined in the CREATES Act are enacted into law, they will supersede the provisions of the draft guidance on waiver of the SSS REMS requirement.

FDA will accept comments on both draft guidance documents until July 31, 2018.

For more information on this topic, please contact a member of our FDA Regulatory team or your usual Ropes & Gray advisor.