Development of Single, Shared System REMS

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What is a REMS?

- **R**isk **E**valuation and **M**itigation **S**trategy

- A required risk management plan that uses risk minimization strategies beyond professional labeling to ensure that the benefits of the drug outweigh the risks.

Possible Components of a REMS

A REMS can include one or more of the following:

- Medication Guide (MG) or Patient Package Insert (PPI)
- Communication Plan (CP) for Healthcare Providers (HCPs)
- Elements to Assure Safe Use (ETASU)
  - For example: prescriber/pharmacist training/certification requirements, patient monitoring requirements, limitations on where/how drug can be dispensed, etc.
- Implementation System

REMS for ANDAs

- If innovator product is subject to REMS, any ANDA referencing that product is subject to these components of the REMS:
  - Med Guide
  - ETASU
    - ANDA must use a ***single, shared system*** with the innovator for any ETASU (unless FDA waives this requirement, in which case ANDA can use different, but comparable system)

Single Shared System REMS

- NDA and all ANDAs
- Single REMS document, REMS materials (except MGs), and supporting documents applicable to all drugs
- Shared database and infrastructure

Benefits of a single shared system

- Reduces burden for different stakeholders
  - single portal to access materials and other documentation and information about the program
  - prescribers, pharmacies, and healthcare settings complete certification and other administrative requirements once rather than for each individual drug
- Potential for cost sharing among all sponsors

SSS Development Process

1. The Office of Generic Drugs (OGD) notifies each ANDA sponsor of the requirement for a SSS by sending a REMS notification letter.
   - The REMS notification letter (1) notifies the ANDA sponsor of the requirement of a SSS, and (2) directs the ANDA sponsor to contact the sponsor of the reference listed drug.

SSS REMS Development Process (Cont'd)

2. ANDA holders make initial contact with RLD holder and initiate discussions about a SSS REMS
3. FDA hosts a "kick-off" meeting to convey expectations and facilitate planning to move SSS REMS development forward

SSS REMS Development Process (Cont'd)

4. Companies may form an "industry working group" (IWG) to develop a proposal for the shared REMS
   - FDA instructs the IWG sponsors to identify a single point of contact to represent the IWG, and emphasizes the importance of first working out the cost and governance structures
   - IWG provides bi-weekly updates to the Agency
5. The Agency forms a REMS review team including staff from a number of Offices within the Center
   - FDA communicates expected timeframes for milestones
   - FDA schedules periodic teleconferences with the IWG

SSS REMS Development Process (Cont'd)

6. Once developed, the SSS REMS proposal is submitted by the innovator and generic companies to the Agency for review.
   - FDA instructs the IWG how to submit the REMS proposal.
7. When a company indicates to the Agency that another company (brand or generic) in the IWG is not receptive or responsive to efforts to develop a SSS REMS, the Agency may serve as facilitator to aid in reaching resolution.

Issues to be Addressed in Negotiations

- Cost-sharing
- Confidentiality
- Product liability concerns
- Anti-trust concerns
- Access to a license for elements protected by patent
- Experience/trust gap(s)

FDA Perspective on Waiver

- Shared system REMS fulfill Congressional intent to reduce end-user burden and foster ease of access to generic products with REMS.
- The waiver provision provides an alternative path for approval of generic drugs if a single shared system is not feasible.
- A waiver is an option of last resort.

Waiver of the SSS Requirement

- Expectation is successful formation of SSS
- If, during the course of negotiations, FDA or the sponsors believe that a waiver may be warranted, FDA will:
  - Determine whether the statutory criteria for a waiver have been met
  - Review a separate proposed REMS submission by the ANDA sponsor(s)

Criteria for Waiver

The Secretary **may waive the requirement** for a drug that is the subject of an abbreviated new drug application, and permit the applicant to **use a different, comparable aspect** of the elements to assure safe use, if the Secretary determines that–

- (i) the **burden of creating a single, shared system outweighs the benefit. . .** taking into consideration the impact on health care providers, patients, the applicant for the abbreviated new drug application, and the holder of the reference drug product; **or**

Criteria for Waiver

…(ii) an aspect of the elements to assure safe use for the applicable listed drug is **claimed by a patent** that has not expired or is a method or process that, as a trade secret, is entitled to protection, and the applicant for the abbreviated new drug application certifies that it has **sought a license for use** of an aspect of the elements to assure safe use for the applicable listed drug and that it was **unable to obtain a license**.

Separate REMS for ANDA(s)

FDA may waive the requirement for a SSS and permit the ANDA to use a "**different, <u>comparable</u>** aspect" of the ETASU

(505-1(i)).

Separate REMS for ANDA(s)

- Same goals
- Same ETASU
  - Contain the same elements
  - Must achieve same level of safety
  - How the elements are operationalized may differ
  - Applicants should explain and justify any differences in operations

Separate REMS for ANDA(s)

Things to consider in developing a separate REMS program:

- Will the operational differences shift burden to other stakeholders?
- Will the operational differences cause confusion for stakeholders?
- Will the operations allow for other ANDAs to join the program?

Waiver Process

- FDA may waive the SSS requirement upon request from a sponsor.
- FDA may determine on its own that waiver is appropriate without receiving a request from a sponsor.
- In each circumstance, FDA conducts an individual analysis based on the statutory criteria for waiving the SSS requirement.

A Complete REMS Submission

- REMS
- REMS Supporting Document
- Appended materials

Proposed REMS

The REMS includes the necessary elements that support the safe use of the product.

- Goals
- Elements to assure safe use
- Implementation system
- Any materials that are referenced in the REMS
  - Training programs -Enrollment forms
  - Patient agreement forms
  - Medication Guide

REMS Supporting Document

- Describe how the program is being implemented
- Whether the element or tools used are compatible with the established distribution, procurement and dispensing systems
- A description of the effectiveness of the proposed program
- Includes metrics that will be used to determine or identify problems with the program and if the goals are being met
- Criteria, methodology or polices that address your management or implementation

Citation and Helpful Links

- REMS Provision in FD&C Act: Section 505-1 (21 U.S.C. 355-1)
- FDA REMS Website: http://www.accessdata.fda.gov/scripts/cder/rems/index.cfm
- FDA Webinar: REMS Basics: http://www.fda.gov/aboutfda/transparency/basics/ucm325201.htm

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