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Risk Evaluation and Mitigation Strategies

In-Home Disposal Systems for Opioids

Lynn Mehler

Partner, Head of Pharmaceutical and Biotechnology practice

Co-head, Life Sciences & Health Care Industry Sector

Hogan Lovells, US LLP

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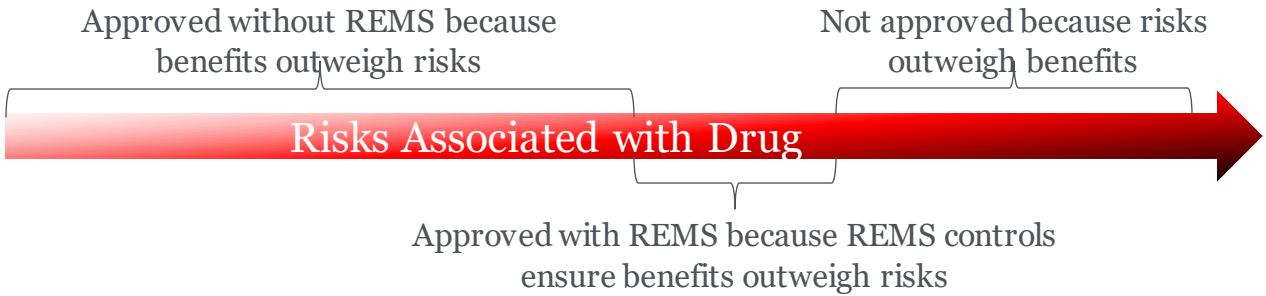
Agenda

- REMS Overview
- REMS Format and Content
- REMS Modification
- Support Act Provisions regarding Packaging and Disposal
- Practical Considerations

REMS Overview

- A **R**isk **E**valuation and **M**itigation **S**trategy (REMS) is required when FDA determines it is necessary to **mitigate** a specific risk to ensure that the product benefits outweigh its risks.



- FDA's authority to require a REMS is limited by the statutory requirement to ensure that the elements of the REMS do not unduly impede patient access to the drug and minimize the burden on the health care delivery.

REMS Overview (Cont'd)

- FDA determines whether a REMS is necessary, specifies the requirements, and approves the REMS and all REMS materials.
- REMS can be required at the time of approval or post-approval
- The Agency also has authority to require elements to assure safe use (ETASU) as part of the REMS to mitigate a specific serious risk listed on the label
- ETASU may include:
  - prescriber certification or training
  - pharmacy certification
  - dispensing of the drug only in certain health care settings
  - dispensing of the drug only with documentation of safe-use conditions patient monitoring
  - patient registry

REMS Overview (Cont'd)

- All REMS must be assessed at an interval determined by FDA to determine if the REMS is meeting the specific goals listed in the REMS.
- A drug is misbranded if its label or labeling are false or misleading in any way(including REMS materials).
  - A drug may be deemed to be misbranded if a sponsor fails to comply with the requirements of the REMS.
  - Introduction of a misbranded drug into interstate commerce may lead to civil monetary penalties, withdrawal of approval or criminal liabilities.
- The statute places the responsibility for REMS compliance on the sponsor (and not stakeholders)
  - REMS are approved with a process to address non-compliance, with decertification as the last resort, particularly given the statutory directive re patient access/burden to stakeholders

REMS Format and Content

- When FDA determines that a REMS is necessary, the sponsor must submit the (i) REMS (REMS Document and Materials) and; (ii) REMS Supporting Document to FDA.
- The REMS includes the REMS Document and REMS Materials –
  - The REMS Document establishes the goals and requirements of the REMS; describes the elements of the REMS and specific steps for each stakeholder to mitigate the serious risk of the drug.
  - The REMS Materials include any materials to operationalize the REMS requirements, such as communication and educational materials, enrollment forms, etc.
  - **Both the REMS Document and REMS materials** must be approved by FDA before they can be implemented and cannot be changed without FDA approval.
  - The REMS Document and materials are enforceable.
- The REMS Supporting Document –
  - Expands on information in the REMS Document and includes the rationale for the design, implementation, and assessment of the REMS.
  - It is not publicly available and represents the "how" of the REMS; how the sponsor will implement and carry out its obligations.
  - The REMS Supporting Document is **reviewed by FDA** at the time of approval of the REMS and when subsequent modifications are made.

REMS Modification

- REMS can be modified either at the request of the sponsor or FDA.
- Changes to REMS range from editorial changes (revisions) to major modifications depending on the degree of effect of the proposed change on:
  - Information in the REMS document and materials relating to serious risk or safe use of the drug; and/or
  - The actions the sponsor, patient, or healthcare providers must take to comply with the REMS
- Major REMS modifications such as adding/removal of a REMS element or tool must be submitted as prior approval supplements (6 month review)
- Minor changes that are editorial in nature can be implemented with notification to FDA.
- Proposed modifications (minor or major) must include adequate rationale for the proposed changes and must be approved by FDA.

Overlapping statutory authorities for controlled substances

Controlled Substances Obligations

- Federal Controlled Substances Act and implementing regs (DEA) and state controlled substances act statutes and regs
- Requires registrations for specific activities and physical locations
  - e.g. Manufacturing, distribution, dispensing, administering
- Requirements for registrants include record keeping, reporting, physical security, limitations on distribution (only to another registrant or end user), and prescription requirements
- A sponsor of a drug product can outsource all activities from manufacturing to commercial distribution of a controlled substance without being a CSA registrant.
- State restrictions/requirements including disposal, prescription limitations, specific taxes

REMS Obligations

- Federal Food, Drug and Cosmetic Act and FDA regs and guidance.
- Tied to mitigating a specific serious risk in the label of the product
- Obligations are drug product specific and appear in REMS document and REMS materials
- Drug product sponsor can outsource activities/activities carried out by stakeholders, but sponsor retains obligations for compliance/reporting (assessment) to FDA

Support Act Provisions

- REMS authority modified by Support Act
- Provides agency authority to require (for certain patients):
  - Packaging to mitigate a serious risk
  - Safe disposal packaging or system
    - Mitigate serious risk
    - Sufficiently available
- Requires agency to take into consideration:
  - Patient access
  - Impact on health care delivery system
    - Be compatible with established distribution, procurement and dispensing system
- Agency must consult with other federal agencies with authority over drug disposal packaging

Practical Considerations for Drug Disposal Systems

- Will it work?
  - DEA standard for rendering unretrievable
  - Patient understanding and actual use
  - Range of settings
  - What products and how to regulate?
- Will it be unduly burdensome?
  - Short term prescriptions
  - Patients with chronic pain
  - Healthcare system impact
    - Pharmacies
    - Sponsors
- Unintended consequences

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