

PHARMACEUTICAL COMMERCE

Business Strategies for
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Dealing With REMS Challenges in Drug Commercialization

Five steps to take when the duty for developing Risk Evaluation and Mitigation Strategies (REMS) is imposed on commercial operations

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THE ADVENT OF THE RISK Evaluation and Mitigation Strategies (REMS) era has fundamentally changed the way many new drugs are launched and safety risks are monitored post-launch. Successful design and implementation of complex REMS programs requires pharmaceutical and biotechnology manufacturers to approach commercialization with uncharted processes and considerations. Planning early for a possible REMS mandate, bringing together key internal stakeholders, securing an experienced vendor to implement the REMS, and seeking ways to realize efficiencies by linking safety and reimbursement programs are all critical factors that influence commercialization strategies and ultimately, REMS program success.

While the vast majority of REMS programs approved in 2008 required only the distribution of a medication guide and assessing patients' receipt and understanding of the guide, a shift in program complexity is occurring. Many REMS currently in development are more stringent than their predecessors, and several include Elements to Assure Safe Use (ETASU). All REMS programs are designed to manage a known and potentially serious risk associated with a drug or biologic, but those programs involving ETASU are

the most complex and may involve physician certification, patient enrollment, ongoing collection of patient data and controlled distribution. These programs impact commercialization most significantly and have far reaching implications for the way drugs reach hospitals, physician offices, pharmacies and patients.

What should a manufacturer do to prepare for a possible REMS mandate?

Step 1: Know the Risk Profile

Anticipating the likelihood of a REMS mandate and the potential scope of the program is an important first step in the planning process.

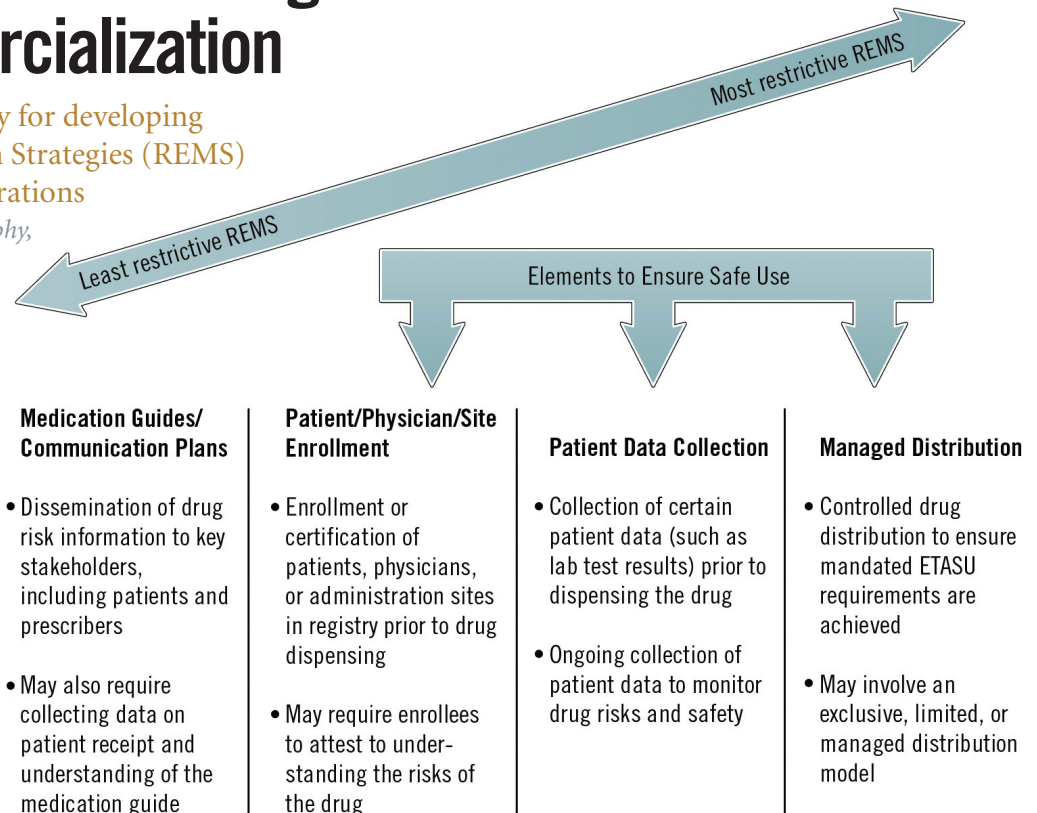


Figure 1: Spectrum of REMS Program Components

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Although the first REMS were mandated by the Food and Drug Administration (FDA) just 16 months ago, early trends, patterns and indicators have emerged. In 2008, two-thirds of new biologic [1] and specialty drug [2] approvals were required to have a REMS as part of their commercialization plan. In addition, drugs with certain risk profiles are more likely to have a REMS than those with less-serious potential side effects. Several drugs with risks related to teratogenicity, cardiac problems, hematologic risks, liver dysfunction and new or worsened malignancies have required a REMS program. Products that treat serious or life-threatening diseases or those that meet a previously unmet medical need may also have an increased likelihood of requiring a risk management plan. Further, commercialized drugs and biologics with emergent adverse-event data accounted for almost 50% of REMS approved last year—a further indication that any drug is subject to REMS if the risk profile is deemed significant.[3]

Manufacturers should look closely at such trends and make early determinations about the probability of a REMS mandate for their pipeline agents.

Step 2: Organize Internally

Getting the right people “around the table” for planning and development is critical.

When the first complex REMS programs were mandated in early 2008, manufacturers were entering entirely new territory and were faced with many critical questions. How will REMS impact our existing commercialization strategy? How should we organize internally for success? What departments should be involved, and what role does each play? While many manufacturers continue to struggle with these questions upon learning that the FDA has mandated a REMS for their product, others have begun to organize for REMS success by implementing various organizational strategies.

When unexpectedly faced with a REMS involving patient enrollment, physician enrollment, institution enrollment and controlled distribution in 2008, a biologic manufacturer approached McKesson to help design the program, prepare required supporting documents for the FDA, assist with conversations with the FDA and implement the program. While McKesson was preparing to operationalize the REMS, the manufacturer began to organize internally to not only meet the needs that this REMS required, but to establish enterprise-wide processes and designate personnel who would be

Top Five Questions For REMS Vendor Selection

1. Have you helped design and implement risk management programs in the past? Are you currently managing any REMS programs?
2. If yes, what components and types of activities are included in those programs?
3. What was your role in the development of those programs, and what is your ongoing role?
4. Detail your specific assets and capabilities. Has your organization managed the following:
 - a. Development and distribution of medication guides?
 - b. Assessments of patients' receipt and understanding of medication guides?
 - c. Patient, physician, pharmacy, or hospital enrollment?
 - d. Ongoing collection of patient data?
 - e. Integrating REMS and reimbursement / access programs?
 - f. Ability to distribute products through specialty pharmacies, retail pharmacies, or both?
 - g. Distributing products in a highly controlled manner?
 - h. Reporting on REMS program data to the FDA?
5. What lessons learned can you share based on your risk management experience?

accountable for preparing REMS for their pipeline products, should it become necessary.

A lesson quickly learned during this process was that a cross-functional team to assist with the development and ongoing support of a REMS must be assembled, and representatives from regulatory, legal, brand, managed markets, technology, training, distribution and clinical research must have a seat at the REMS table. Further, gaining commitment from all levels of the organization to support the REMS was important to facilitate program design and the development of commercialization strategies.

For manufacturers with pipeline products whose risk profiles suggest the likelihood of a REMS, creating a dedicated team to manage existing and future risk management programs may make sense. Regardless of the approach or struc-

ture, past lessons have shown that effective internal organization and resourcing for REMS are key factors for commercialization success.

Step 3: Plan Early

Developing a risk management plan before mandated by the FDA may be a wise strategy.

As REMS become more common and manufacturers face the possibility of several months of drug launch delays when notified of an unexpected REMS requirement, many are planning early and preparing a risk management plan as an “insurance policy” in the event that the FDA requires it at the time of launch or post-commercialization. In some cases, organizations are implementing risk management programs at the time of launch, regardless of whether the FDA mandates it, to ensure patient safety and avoid preventable adverse events.

Planning early and developing a risk management plan prior to New Drug Application (NDA) submission allows manufacturers the time needed to consider the impact REMS would have on commercialization and prepare strategies to effectively balance risk and access. This approach also affords the opportunity to organize internally and create a cross-functional team to support risk management activities, as well as prepare a timeline and budget to support the REMS.

Step 4: Select the Right Vendor

Partnering with an experienced vendor that has implemented and managed complex REMS and can support all components of the program is highly beneficial.

No two REMS programs are alike. Each approved REMS has a unique design and methodology for meeting FDA requirements, just as the drugs they support have distinct risk profiles that must be effectively managed. As Fig. 1 demonstrates, a REMS can be as restrictive as a controlled distribution model with patient, physician and institution enrollment and the ongoing collection of patient data or as simple as the distribution of a medication guide.

Determining whether the REMS will be designed and managed in-house or whether the organization will outsource the REMS to a vendor is one of the most important decisions a manufacturer must make. Although a small number of pharmaceutical and biologic manufacturers are organized to man-

age less restrictive REMS programs in-house, the vast majority are not structured to manage the more complex components often required by the FDA. Further, while a REMS may start with the straightforward distribution of medication guide, the requirements of the program could potentially expand if new risk or adverse-event data emerge or if the program is not meeting its goals.

When outsourcing the development and implementation of a REMS, manufacturers must carefully select the most appropriate vendor to manage the programs’ unique requirements. A careful evaluation of potential partners’ capabilities and experience is critical. Fig. 2 highlights the most important questions manufacturers should consider when selecting a REMS vendor.

Step 5: Linking REMS and Reimbursement Programs

Evaluating opportunities to link safety and access programs may help ease the burden on physician offices and create cost efficiencies.

One of the primary concerns associated with REMS programs is the additional work required of physician offices. Physician enrollment in REMS programs and completion of the required physician certifications or trainings takes time away from patients and creates a hurdle for appropriate drug adoption. Manufacturers can ease the burden on physicians by integrating REMS and reimbursement initiatives.

As described, biologics and specialty drugs are the most likely REMS candidates. Due to these products’ high costs and out-of-pocket spending requirements, patients taking these drugs are most in need of reimbursement assistance. Typically, the burden is on the physician’s office to seek and obtain prior authorizations, benefits approval and reimbursement assistance for their patients. If these same physicians are also required to enroll in a REMS for the same drug, manufacturers can create a single point of contact through which both reimbursement and REMS needs can be managed simultaneously.

This approach helps minimize the administrative workload required for physician practices to safely prescribe, administer and obtain reimbursement on behalf of the patient. Selecting a vendor that has experience managing both REMS and reimbursement programs may also create process and cost efficiencies for manufacturers by leveraging a single framework and system to manage both programs.

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Looking to the Future

REMS are perhaps the most significant change to U.S. drug regulation in many years. With risk management plans becoming more common and complex, planning early for a possible REMS mandate has never been more critical as manufacturers are facing significant and costly drug launch delays if unprepared. Bringing together key stakeholders within the organization throughout the program development phase and gaining support from all levels of the organization is crucial. Creating a single point-of-contact for both REMS and reimbursement programs can help minimize the burden on physicians' offices and potentially increase adoption of the product. Manufactur-

ers should also carefully select a vendor with broad assets and proven capabilities to help guide them through the program design and FDA submission process, as well as implement the spectrum of program components. REMS is here to stay, and now is the time to embrace risk management planning as an integral part of the commercialization process. **PC**

REFERENCES

- 1 Smith, L. "The REMS Report Card: FDA Using New Tools for One-Third of New Drugs in First Six Months," *The Pink Sheet*, November 10, 2008.
- 2 Analysis of FDA approval data, 2008.
- 3 Ibid.

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