WHITE PAPER

Lessons Learned When Implementing a REMS Program

120 REMS Programs and Counting

UBC

The Best Indicator of a Future REMS is a Past REMS

Insights into the type of REMS program which may be required can be found by understanding REMS already in the marketplace, particularly those recently approved and those with similar indications or similar risks. Based on our extensive experience, UBC not only understands FDA's criteria for REMS approval, but we can also provide insights into new approaches which FDA is considering and those which they have rejected. For some products, the FDA has required Shared System REMS; for these, multiple sponsors must operate together under one REMS. UBC's work on these programs has provided our team with valuable strategies for seamlessly working across multiple competitors.

A successful REMS program will direct the right therapy to the right patients at the right time.

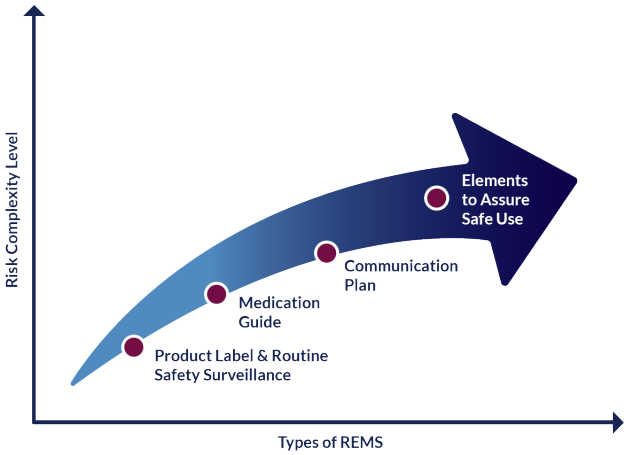
REMS Must Align with the Healthcare System

Most of the currently active REMS include one or more Elements to Assure Safe Use (ETASU), which ensure safety measures are in place before patients receive their medication.

REMS with ETASU may require:

- Prescriber and pharmacy training and certification.
- Patient monitoring to ensure safe use conditions prior to and during treatment.
- Patient enrollment and long-term follow-up while the patient remains on the medication.

Figure 1: Risk Mitigation Strategies



As shown in Figure 1, as the risk mitigation needs of a product increase, the complexity of REMS requirements also increases.

There is often the perception that a REMS implies a product is "dangerous," thereby impacting healthcare providers' willingness to prescribe. If a REMS is constructed and executed appropriately, the likelihood that a healthcare provider will prescribe can increase because the prescribers are well-informed, the benefit/risk of the product has been clearly communicated, and guidance is provided about appropriate product use and risk minimization.

A REMS program must also integrate efficiently into the healthcare system. It is not just important to look at the requirements to achieve approval; it is just as important to look at the viability of the program in the marketplace.

Viability is driven by an in-depth understanding of:

- The usual workflow in healthcare provider practices.
- How and where decisions about therapy initiation are made and who makes them.
- How and when patients access medication, and
- What processes and technologies are used to prescribe medications.

The answers to these questions can differ in each healthcare setting and for each patient population.

Lessons Learned

Working with many stakeholders and patient populations across a wide variety of therapeutic areas has taught us valuable lessons about REMS programs and product safety, including:

PLANNING FOR RISK MITIGATION STARTS EARLY

Proactive risk management should begin early in the development process allowing for opportunities to:

- Understand the product safety profile.
- Determine if risk mitigation strategies will be incorporated into clinical trial protocols.
- Understand how the clinical trial population may differ from the post-approval target population and any implications this has for a successful REMS.
    - The patient population treated as per usual care after marketing will include patients on multiple concomitant medications and patients in special demographic groups, such as the elderly or women of reproductive potential, who may not have been well-studied during the development program.

COMMUNICATION AND COLLABORATION ARE KEY

Determining which risk factors and the level of risk that may impact the benefit-risk balance of a product requires input from many different groups within a biopharmaceutical company, as well as from regulatory agencies, patient advocacy groups, healthcare providers and patients.

AIM FOR INNOVATION IN EDUCATION

REMS have brought many innovations to the marketplace, including innovative tools for patients, prescribers, pharmacists, and distributors to communicate risk. Develop and test strategies that educate stakeholders in a clear and comprehensive manner and make educational tools easily accessible.

PATIENTS MATTER MOST

Appropriate safety guidelines are necessary. If requirements are too complicated and cumbersome for patients and their prescribers to follow, it's possible another product or course of therapy may be chosen.

PLAN AHEAD TO EVALUATE REMS EFFECTIVENESS

Various prospective and retrospective methods exist to evaluate the effectiveness of the REMS once it has been implemented. Early planning to anticipate potential designs and operational strategies will allow for a more efficient and timely evaluation.

History of a REMS

The Food and Drug Administration Amendments Act (FDAAA) of 2007[1] heightened the industry's approach to product safety by giving the Food and Drug Administration the authority to require Risk Evaluation and Mitigation Strategies (REMS) for new and existing products to ensure that the benefits of a drug or biologic outweigh its risks.

REMS requirements may include Medication Guides - easy-to-understand patient labeling with information about serious side effects - Communication Plans that involve notifying and educating healthcare professionals about a product's safety information, and Elements to Assure Safe Use (ETASU). ETASU may involve healthcare provider and pharmacy certification, patient enrollment, and instituting and monitoring safe use conditions.

Before REMS were required, the industry utilized Risk Minimization Action Plans (RiskMAPs) and Performance-Linked Access Systems (PLAS) to ensure necessary restrictions were in place for the safety of patients. UBC scientists developed one of the first PLAS instituted in 1999. That program, for a drug that treats patients with schizophrenia, is still in effect today as a REMS.

Summary

With the experience of more than 120 RiskMAPs and REMS programs for products in a variety of therapeutic areas, UBC recognizes what is needed for product approval, patient safety, and commercialization. We welcome the opportunity to further explore ways we can apply the lessons we have learned to help you navigate your product through regulatory and commercial requirements so it can reach the right patients under the right conditions to optimize care.

UBC has played a significant role in patient and product safety. Our teams of epidemiologists, safety scientists, data analysts, software developers, and patient educators have designed, implemented, and evaluated RiskMAPs and REMS programs to treat everything from diabetes to organ transplant rejection.

About UBC

United BioSource LLC (UBC) is the leading provider of evidence development solutions with expertise in uniting evidence and access. UBC helps biopharma mitigate risk, address product hurdles, and demonstrate safety, efficacy, and value under real-world conditions. UBC leads the market in providing integrated, comprehensive clinical, safety, and commercialization services and is uniquely positioned to seamlessly integrate best-in-class services throughout the lifecycle of a product.

Connect with us to learn how UBC's comprehensive safety & risk management solutions can improve the quality and efficiency of your REMS program.

About the Authors

ANNETTE STEMHAGEN, DRPH, FISPE

Chief Scientific Officer

Multidisciplinary approach to evidence generation strategies with a focus on epidemiology, safety surveillance, and risk evaluation and mitigation strategies.

RACHEL BONFANTI

Senior Director - Risk Management & Scientific Consulting

Risk Management strategy design and interdependency management of risk evaluation and mitigation strategies programs.

References

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contact@ubc.com

ubc.com

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