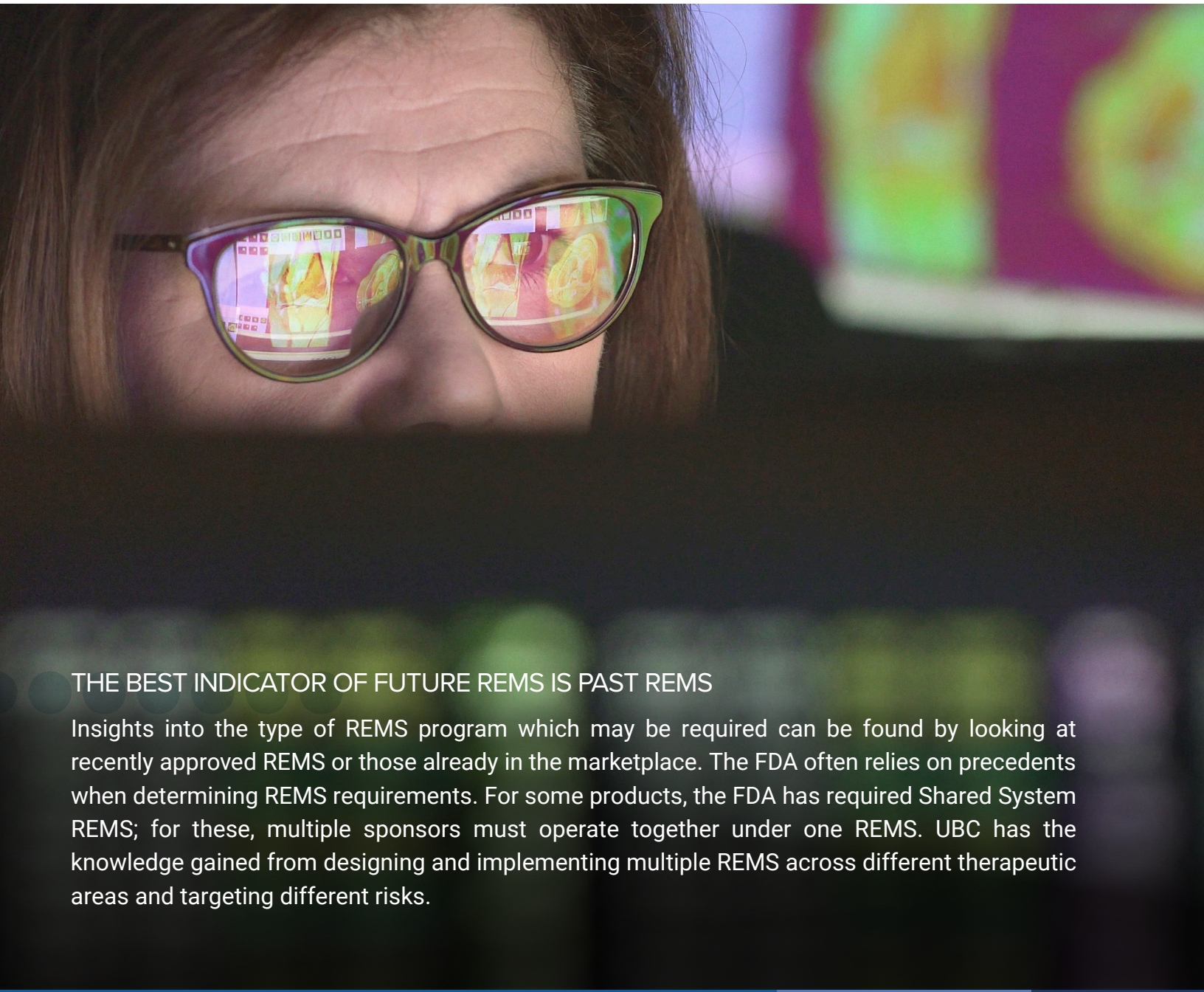
WHITE PAPER

Lessons Learned When Implementing A Risk Management Program:
120 REMS Programs and Counting



THE BEST INDICATOR OF FUTURE REMS IS PAST REMS

Insights into the type of REMS program which may be required can be found by looking at recently approved REMS or those already in the marketplace. The FDA often relies on precedents when determining REMS requirements. For some products, the FDA has required Shared System REMS; for these, multiple sponsors must operate together under one REMS. UBC has the knowledge gained from designing and implementing multiple REMS across different therapeutic areas and targeting different risks.

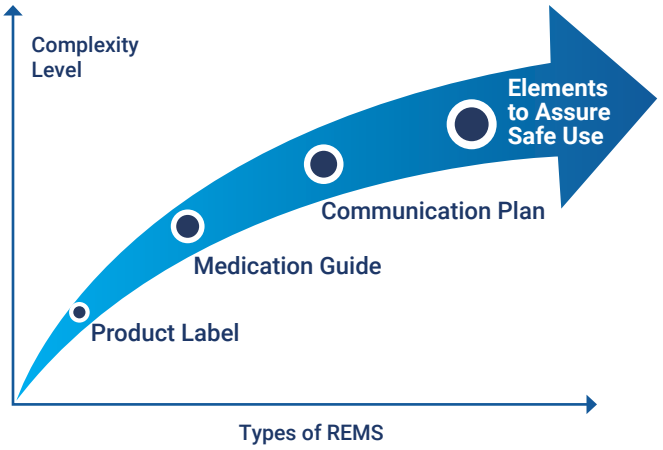
REMS MUST ALIGN WITH THE HEALTHCARE SYSTEM

Many products with REMS include Elements to Assure Safe Use (ETASU), which ensure additional 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 while the medication is being used.
- patient enrollment and long-term follow-up while the patient remains on the medication.

RISK MITIGATION STRATEGIES



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

There is often the perception that a REMS program implies a product is "dangerous", thereby impacting healthcare providers willingness to perscribe. If a REMS program is constructed and executed appropriately, the likelihood that a healthcare professional will prescribe can actually 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 that neglects to consider how best to minimize product risk can place a burden if it does not 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.
- what processes and technologies are used to obtain 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 many 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:

- begin compiling the product safety profile.
- determine if risk mitigation strategies have been incorporated into clinical trial protocols.
- understand how the clinical trial population may differ from the post-approval target population.
    - 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 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 improved education of patients, prescribers, pharmacists and distributors. Develop 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 heightened the industry's approach to product safety by giving the Food and Drug Administration (FDA) the authority to require Risk Evaluation and Mitigation Strategies (REMS) for new and existing products.

Currently there are select products on the market requiring a REMS 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: Elements to Assure Safe Use (ETASU).

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.

About UBC

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 patient 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.

UBC leads the market in providing integrated, comprehensive clinical, safety, and commercialization services. UBC is uniquely positioned to seamlessly integrate best-in-class services throughout the lifecycle of a product.

By Annette Stemhagen, DrPH, FISPE Senior Vice President and Chief Science Officer, Safety, Epidemiology, Registries, and Risk Management

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