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The dynamic evolution of multi-sponsor REMS

Risk Evaluation & Mitigation Strategy (REMS) programs are evolving, with new complexities for compliance managers

By Frank Gallo and Robin Kinard, PPD

Are you prepared to work with your competitors on the development, management and assessment of a Risk Evaluation & Mitigation Strategy (REMS) program for your drug or biological product? If you have a REMS now or may have a REMS program associated with one of your products in the future, there is a good chance you will eventually be doing just that.

REMS are programs mandated by FDA that are designed to minimize one or more product risks with one or more tools. REMS have become part of daily life for pharmaceutical companies, healthcare providers, patients and distributors since 2008. During this time, there have been a variety of REMS program challenges and changes. Incorporating these programs successfully and effectively into the commercialization of products requires a continuous effort from multiple stakeholders to adapt to the ongoing changes and rise to the program challenges.

In this article, we will provide a brief background of REMS programs; describe dramatic shifts in the types of REMS approved; explore the challenges associated with multi-sponsor REMS; and discuss how to ensure that your company and your company's products are prepared for a continually changing environment.

FDA mandates REMS for certain pharmaceutical products to minimize one or more specific product risks. Prior to the introduction of REMS in the 2007 Food and Drug Administration Amendments Act (FDAAA) and the initiation of these programs in 2008, Risk Management Programs and Risk Minimization Action Plans (RiskMAPs) were used to manage these risks. In fact, FDA deemed 16 of these older risk management programs to be, in effect, REMS in 2008. Although FDA does continue to approve some products under RiskMAPs, REMS have become the most commonly approved type of program.

Evolution of program types

Beginning in 2011, the types of REMS programs being approved and the number of programs on the market have been changing radically. Up to that time, FDA had been publicly stating that its goal was to move toward multi-sponsor REMS to reduce the burden on healthcare providers by reducing duplicative effort. However, the complexities added by having multiple sponsors negotiate, implement and assess programs in unison delayed the adoption of this approach. As experience grew with REMS, the intended trend toward multi-sponsor REMS began. The dramatic shift since 2011 is illustrated below (Table 1).

Put another way, through 2010 less than 3% of products with approved REMS were part of a multi-sponsor REMS; today, according to data on the FDA REMS website, 44% of products with REMS are part of a multi-sponsor REMS program.

The impact of this shift on pharmaceutical companies has been significant. Some companies had just begun to establish how they would manage REMS programs internally and which departments would be responsible for each deliverable, but now they are being forced to integrate their processes with other drug sponsors that are typically direct competitors.

This shifting dynamic has created a need for increased resources from internal personnel, as well as external service providers, including resources and technologies that allow for multiple sponsors to work together in a fair and transparent manner. At PPD, a global contract research organization serving the biopharmaceutical industry, we work on many single-sponsor and multi-sponsor programs. This experience provides insight from lessons learned in this rapidly evolving space.

Lessons learned:

- Pharmaceutical companies should identify a lead department (usually regulatory, medical/safety, or commercial) to coordinate the activities of all departments within the company for REMS programs and ensure that all communications are effectively delivered and tracked.

Table 1. Multi-sponsor REMS are growing

	Through 2010	Today
Products under approved single-sponsor REMS	178	65
Products under approved multi-sponsor REMS	5	51
Percentage of products with approved REMS that are part of a multi-sponsor REMS	2.8%	44%

(Continued)

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- Processes for sharing communication in real time, or as close as possible, should be implemented.
- When programs are designed, the assessment plan must be designed at the beginning with the goals, so that key performance indicators (KPIs) and key quality indicators (KQIs) for each component of each program are determined at the start and tracked from Day One.
- Companies must assume REMS programs will require an ongoing commitment (financially and from human resources) as long as the product is marketed.

Impact on service providers

REMS programs have required service providers that support pharmaceutical companies to evolve, as well. At PPD, for example, we have invested in a REMS department that leverages the wide range of resources in our organization to meet the varying needs of our REMS clients. Additionally, PPD partnered with Caradigm to jointly invest in and create the first REMS technology platform. (Caradigm is a joint venture between Microsoft and GE Healthcare focused on health data management.) These investments were necessary to proactively prepare for the changing needs in the marketplace and have provided the operational model and cutting-edge technology necessary to support our current and future clients.

Just as pharmaceutical companies have been required by FDA to work with competitors to develop, implement and assess REMS programs, pharmaceutical services providers need to work with their direct competitors to support REMS programs. Direct competitors are now becoming sub-contractors to each other to accommodate the need for multi-sponsor consortia to have a single point of management for the complex programs.

PPD's exclusive REMS technology has become especially valuable for multi-sponsor programs by providing each department of each sponsor company with the same information about the operations, metrics and documents of the program in real time. At the same time, the prescriber, pharmacy and patient-facing components of the REMS run directly from the program; thus, ongoing management and assessment can be performed efficiently through a user-friendly interface (Fig. 1).

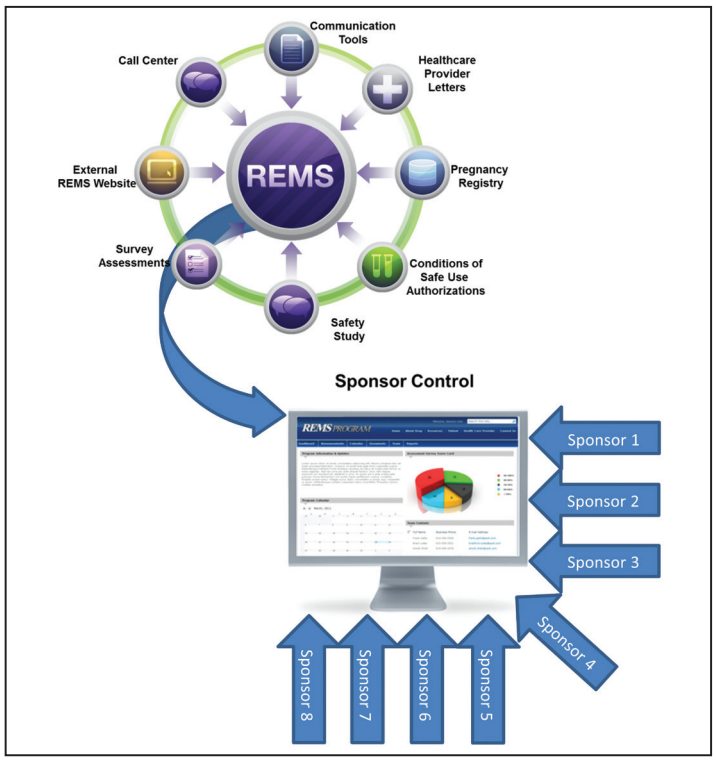

Fig. 1. The structure of PPD's REMS management system. Credit: PPD

Impact on healthcare providers and patients

The impact of REMS on healthcare providers and patients has continued to be an increasing burden. Although the trend toward multi-sponsor REMS does reduce the total number of programs and keeps healthcare providers and pharmacists from a requirement to learn multiple programs for branded and generic (or similar) products, these stakeholders do not necessarily realize any reduction in what is being asked of them.

The reality is that healthcare providers and pharmacists have more responsibilities each year as new REMS are approved. However, those increases are not as extreme as they would be if the 116 products currently approved under REMS were all under single programs instead of 51 of them being consolidated into six multi-sponsor programs.

How multi-sponsor consortia work

In light of the evolving landscape and trends toward multi-sponsor programs described above, it is important to consider how to ensure that your company is ready to successfully integrate into a multi-sponsor REMS program. Specifically, you should prepare by focusing on three areas:

- Understanding how multi-sponsor REMS consortia work
- Selecting a team from your company to work on the multi-sponsor REMS
- Structuring a sustainable and appropriate operational model and processes

There are currently six multi-sponsor REMS consortia with approved programs, while additional consortia are working to gain approval. Although there are differences in how the consortia are structured and work, there are also similarities.

When consortia form, commonly they jointly establish the processes and rules they will follow to govern themselves and make decisions. These generally culminate in a central agreement that each of the member companies signs to officially join the consortium. This agreement also addresses items such as how disputes will be handled, how anti-trust issues will be avoided and how members, both at the time of program development and in the future, will pay for the program.

Once agreement on the processes and rules is reached, the consortium members usually establish representatives from each company who have the authority to vote for their respective companies and set up committees to manage different parts of the program (e.g., regulatory, vendor management, operations, finance, etc.).

A consortium generally selects a vendor to be the program management office (PMO) service provider. This PMO vendor typically handles the vendor selection processes for other vendors, provides the consortium a single point of contact for all vendors, and represents a single point for the budget for all programs. The PMO office coordinates the consortium meetings and committee meetings, and also coordinates vendor deliverables.

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Building your team

There is a clear need for companies to enter these consortia with a solid understanding of the commitment required and a team selected for successful participation. The size and structure of the team will be driven by the size and structure of the specific consortium being joined; however, there are some consistently necessary actions:

- Select an individual in your company to be the lead representative for the consortium. This person may come from regulatory, medical, operations or other departments but must have access to all appropriate departments within your organization. He or she will vote on behalf of your organization and manage the team of individuals from your company participating in the REMS. This will require a substantial time commitment.
- Determine a team across regulatory, legal, commercial, finance, medical and other internal departments that will support the program. The team members will work with the leads from other companies in their respective areas of the REMS and in all probability will participate in one or more of the consortium committees.
- Prepare an approval process for making consortium decisions that require executive management approval (e.g., contracting issues, financial decisions, and FDA negotiations).

Once your internal team is in place and the consortium is being formed, it is critical to the immediate and long-term success of the program to institute effective processes and procedures. Although many of the core structural parameters will be outlined in the initial agreement among the consortium members, the actual build and operations of the program will be driven by the consortium members.

Specifically, each member of the consortium should have the same access to the same information in real time or near real time. One way to accomplish this real-time information sharing is the REMS platform described above, developed by PPD and Microsoft; however, the important thing is to have a process and technology in place regardless of the service providers supporting each consortium.

Without these processes in place, the members of your team supporting the program will not have access to the information they need to make informed decisions. Additionally, their counterparts at other companies may or may not be working from the same information in making decisions as the members of your team.

In conclusion, the dramatic shift toward multi-sponsor REMS in the past few years necessitates that companies with existing or future REMS for their products be prepared to participate in a multi-sponsor REMS. The percentage of products with approved REMS programs that are part of a multi-sponsor program has shot up from 2.8% at the end of 2010 to 44% today, and indications are that this trend will continue.

This dramatic shift has affected pharmaceutical companies, service providers, healthcare providers and patients alike. Pharmaceutical companies and their services providers specifically have needed to work closely with competitors on a daily basis. Company-specific and joint processes and procedures have also been necessary in order to manage the development, operations and assessment of the REMS program as consortia as opposed to individual companies.

As companies continue to participate in or join these multi-sponsor programs, there will be new lessons learned, and evolution in this dynamic area will continue. PCm

ABOUT THE AUTHORS

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