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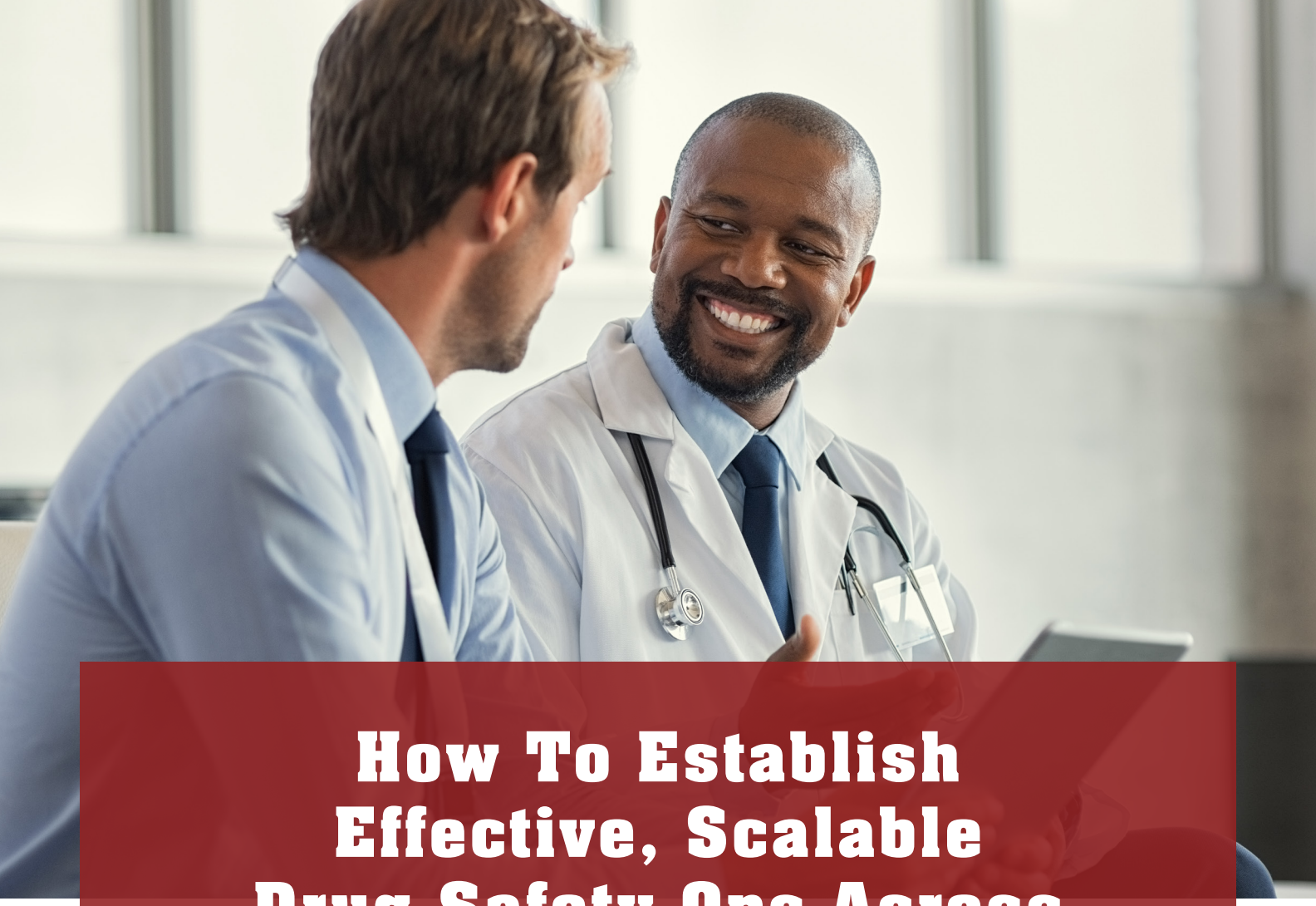

How To Establish Effective, Scalable Drug Safety Ops Across Multiple Vendors

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Drug safety is not a tangential, departmental concern in clinical trial operations; it is the cornerstone of an effective clinical trial designed to pass regulatory muster. Successful drug safety programs are marked by a collaborative dynamic and lead to both operational and financial efficiencies.

Often, the catalyst for safety program issues — the most common and critical of which is non-compliance with safety reporting regulations — is the use of multiple safety vendors. Although working with a single safety vendor is typically ideal, even across multiple clinical trials, it can be difficult to accomplish. Thus, it is important to enlist a combination of strategies and tools to help navigate the challenges that arise from bringing together multiple safety vendors within one or more investigational medicinal product (IMP) development programs. While numerous factors impact a drug safety program, proper management of three key program elements drives success while creating a scalable drug safety model for future programs.

1. Data Listings And Formats

Data listing and format problems arise when different vendors use different safety systems. Although each of these systems is compliant by itself, creating a comprehensive safety assessment deliverable requires consolidation of those systems' data to ensure clarity and brevity for regulatory reviewers.

Consider the development safety update report (DSUR) as an example of such a deliverable. The DSUR has a required format for both listings and the core document. Different safety systems will generate compliant listings for the DSUR, but those listings are not identical; field names or order can vary. So, the sponsor or vendor writing that DSUR must collect safety data outputs from all safety vendors and consolidate those into a single data set, providing regulators a comprehensive safety profile picture.

Manual consolidation of safety data requires rigorous quality control to ensure the data's integrity. Depending on the volume of data, this can take weeks, including time spent asking questions of each contributor to confirm the information presented is accurate.

A trio of strategies can help sponsors to overcome disparate data listings and formats. First, sponsors can share data formats/templates during implementation/onboarding of each safety vendor to ensure alignment. This effort is assisted by insisting that each safety vendor provide a milestone road map for the coming year: key deliverables, timelines, planned discussions, and (if necessary) information sharing with other safety vendors. It is vital that the sponsor has oversight of the entire program. For example, if the program undergoes serious adverse event (SAE) reconciliation every three months, the safety vendor should provide a set schedule so that task can be aligned with sponsor/vendor data management, clinical operations teams, and medical monitors/reviewers.

Second, the sponsor should establish a standard onboarding process for new safety vendors. Use a checklist for those vendors developed by a provider-supplied pharmacovigilance (PV) consultant or an independent PV consultant. Third, sponsors should attempt to utilize a central safety vendor for all studies or multiple vendors who utilize the same safety system.

Utilizing a single database will stave off many potential problems and create a scalable model to add new studies to the same database. While DSUR served as an example deliverable above, the same logic applies to analysis of similar events, coding conventions, and signal detection. The sponsor will not have to finance a new configuration for the database when adding new studies, and the same database will remain usable as the project transitions to post-marketing phase.

2. Processes And Conventions

Different vendors often follow different processes, adhere to different timelines, and use different document templates. This poses a challenge for sponsors reviewing those documents during implementation, attempting to make sure the new vendor's practices align with the program's other safety vendors. Sponsors struggle to juggle the differences between the study teams as well. For example, partnering with three CROs/service providers typically means working with three clinical operations project managers plus, perhaps, three safety team-specific project managers. Roles and responsibilities can get muddled, and it can be difficult to ensure everyone has the same information at the same time.

Sponsors are accountable for their drug's safety profile and for compliance in safety reporting, but they are well served to seek a safety vendor that grants them some authority over how different processes are conducted, allowing those processes to be centralized

consistently. The sponsor should be able to drive customization of the vendor's existing document templates to better align them with what the sponsor already has in place.

For example, when reviewing an SAE report across vendors, they may use different narrative templates, or one uses a chronological narrative while another uses an integrated narrative. The sponsor should have some influence on those choices. Accordingly, one solution to process and convention issues is to use standard document templates developed by an independent or CRO safety consultant that will be used by all safety vendors within the IMP development program.

Another solution to avoid process and convention problems is to hold a regular, centralized safety meeting for all vendors. A fundamental tenet of effective team management is giving people a place where they know they will hear vital information. Standing agenda items will prompt notification of key program updates, including new country approvals, newly approved investigator sponsored trials (ISTs), updated investigators' brochures (IBs), and upcoming aggregate report data lock points (used as the basis for DSURs). It is prudent to maintain minutes from these meetings, allowing the sponsor to show how information has been communicated with and shared among safety vendors, who participated, and that the sponsor provided oversight.

3. Cross Reporting

Cross reporting can seem like a minor issue at first, but one of the biggest clinical trial pain points is misaligned timelines and due dates between vendors. To ensure compliance, timelines across all vendors must be aligned. As a result, one or two vendors often get "the short end of the stick" in that they are forced to produce their reports early to meet the timelines established by other safety vendors. So, each vendor is responsible for expedited reports on the trial they're managing, but the sponsor must oversee communication and ensure cross reporting is completed across all trials.

However, overseeing multiple vendors across multiple programs can get out of hand quickly as the trial begins adding factorials; it becomes an exponential problem, rather than a linear one. A single event must be reported to many places, and the tracking of submission and documentation distribution can be burdensome.

One way to reduce such issues is to share the timelines and reporting requirements of each vendor with all other vendors. This fosters alignment and timely distribution of required deliverables by helping to ensure each safety vendor meets its reportability timelines to other partners. This can be difficult because competing vendors may not want you to share information in their safety management plan (SMP), but it remains important to share their non-regulatory (e.g., contractual) requirements. For example, during ISTs or compassionate use, timelines and reporting requirements need to be disseminated to anyone treating patients or subjects with that IMP. The involved parties must move past the competitor issue and prioritize public safety; there are no industry secrets anymore in PV and drug safety.

A good way to gauge the effectiveness of current practices and to identify opportunities for improvement is to hold a suspected unexpected serious adverse reaction (SUSAR) "pressure test" that includes all involved parties A quick virtual "walk-through" of a SUSAR report workflow, communication flow, and reporting activities provides the sponsor an idea of each vendor's readiness as well as their ability to communicate and work together.

Subpar Safety Tarnishes Trials

Organizations and individuals overseeing safety across multiple clinical trials need to think of drug safety as more than just SAE case processing. Drug safety is an integral part of all trial activities. Formal decisions regarding trial milestones (e.g., dose escalation) are frequently made based on safety data that has been reported. Regulators make key decisions in development and approval of new medicinal products and devices based on collected safety data. Problems are on the horizon if clinical operations, safety vendors, and, to some extent, regulators are not having early and frequent conversations about drug safety and how it will come together holistically.

It's not enough for safety vendors to show potential clients a presentation detailing how they process cases. Effective safety vendors explain exactly how much and what kind of support they will provide the sponsor. Such vendors are clear about process flexibility and their availability as well as whether they will provide a central contact for the sponsor, including details about that person's experience with the program's current stage of development and with organizations of similar size.

Such a partner may sound like the drug safety unicorn, but they do exist. Adept safety vendors are set apart by personnel who look at project hygiene as a whole and consider communication across the entire development program. Their presentation and/or bid defense should address the three elements discussed here — data listings and formats; processes and conventions; and cross reporting — and discuss how the vendor will align those common problem areas with other vendors on the program as well as ensure transparency with the sponsor.

Finally, consider project scope; do not over-engineer solutions. A small, low-volume trial may function just fine utilizing a manual approach to reconcile several SAEs. Look for a safety vendor that wants to understand your needs and fit appropriate solutions, rather than pushing you to shoehorn into a comprehensive but ill-fitting solution to those needs. To learn more, call:

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About The Authors

Rosa Lee Smith is the Vice President of Drug Safety at inSeption Group. With 20+ years of experience in CROs and small biotech companies, Rosa Lee has designed, developed, and implemented more than 250 pharmacovigilance programs across a range of regulatory environments. She applies an innovative and collaborative approach to drug safety and PV from development through regulatory approval, including post-approval regulatory commitments. She has worked on clinical and post-marketing programs for a broad range of products and therapeutic areas, including small molecules, biologics, and orphan drugs for rare diseases. In her role at inSeption, Rosa Lee oversees the drug safety department. Under her strategic leadership and operational support, inSeption will continue to deliver effective and efficient safety-related solutions to aponsors and vendor partners.

Raul P. Lima is Executive Vice President of Clinical Operations at inSeption Group. He is a proven leader in clinical operations with over 20 years of strategic, tactical, and hands-on experience in the management of global, multi-center clinical trials. He has extensive experience with timeline, clinical trial budget, and people management, and has successfully led cross-functional teams, including at CROs. Raul has repeatedly executed strategies ensuring that clinical operations activities supporting clinical trial management are conducted effectively and efficiently, are quality-driven, and comply with all applicable regulations. He possesses an uncanny vision and expertise in communicating that vision to influence strategies that progress cross-functional projects, as well as an unwavering passion for championing development.

Elizabeth Delmaestro, RPh, PhD, earned her B.S. in Pharmacy and her PhD in the Pharmaceutical Sciences from St. John's University. She has been in industry for 30 years and held positions in Toxicology, Clinical Supplies, Medical Information and Drug Safety. She was the Head of Drug Safety in her last two full-time positions. Elizabeth has been an independent consultant for 8 years and provides services including performing gap assessments, setting up signal detection programs and safety governance boards, writing PV SOPs, and acting as the interim Head of Safety.

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