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Safety & Regulatory Solutions for Small and Medium Sized Life Science Organizations

A key issue for small and medium-sized enterprises (SMEs) is the optimal utilization of their limited resources for moving their product pipeline through clinical development, and launching and marketing their approved product(s). This is further aggravated as both clinical trials and post-marketing activities continue to grow in complexity and scope due to stringent regulatory pressures, patient involvement, and globalization. Yet companies face overwhelming pressure to get their product to market as quickly as possible.

Clinical trials are typically outsourced end-to-end to full service Clinical Research Organizations (CROs). SMEs may select CROs for their niche patient recruitment capabilities in certain geographies and Therapeutic Areas/indications. As a result, some CROs may not always have the required level of expertise and experience in other aspects of clinical trials, such as data management, statistical design and analysis, medical writing and regulatory submissions.

Another challenge is that trials may be outsourced to several CROs meaning that safety and pharmacovigilance (PV) activities, along with the technology infrastructure that supports it, are thus housed at multiple CROs as part of their clinical trial programs. This often leads to safety data being reviewed and reported for each clinical trial rather than being reviewed and analyzed at the aggregate (product) level, and data are often collected in different systems resulting in a lack of integration with little or no control over data standardization. This puts organizations at risk at the time of filing of a new drug application to obtain marketing authorization, when it's important to review and analyze consolidated data, define the initial product label, and proactively identify and manage safety concerns.

In the post-marketing phase, many small to medium companies find that it is not practical to have internal resource-heavy, end-to-end safety and risk management system as it diverts extensive time, effort and financial spend away from a company's core activities of product development and marketing. Oftentimes, such organizations do not have an established Safety group and either the Clinical Development or Regulatory groups are responsible for safety activities, leading to lack of focus on critical PV activities. Clinical and regulatory activities in the post-approval phase for registration in different markets and evaluation of safety, efficacy and effectiveness for sub-groups and for other indications can also be quite resource-intensive.

Embracing Newer Strategies

Within the clinical trial environment, a comprehensive understanding of the safety profile of a product often requires evaluation of safety data across all completed and ongoing clinical trials, as well as of any other drugs in the same class. Thorough review and analysis of all aggregate data in real time is particularly important in the context of the US FDA's guidance for IND safety reporting. This timely reporting of meaningful safety information allows the FDA to consider whether any changes in study conduct should be made beyond those initiated by the sponsor and allows investigators to take any essential steps to protect subjects.

Establishing a comprehensive PV organization in-house can be challenging for SMEs. This is because dedicated and experienced professionals are required to manage both PV operations as well as the enabling technology architecture/infrastructure. On the technology side, implementing validated, regulatory-compliant PV systems requires significant investment in a robust quality management system (QMS) and the right expertise to select, implement and support the right solution(s). Yet, the volume of the safety data is often relatively low and volume surges highly unpredictable, therefore, not always justifying the expenditure.

Similarly, on the PV operations side, associated responsibilities such as aggregate safety reporting, benefit-risk evaluation, signal detection and management and development of risk management plans are becoming more complex and resource-intensive. Across Europe and several other countries (including Australia, Canada and Japan), specific regulatory mandate to have Qualified Person responsible for PV (QPPV) and local persons responsible for PV poses additional operational challenges to SMEs.

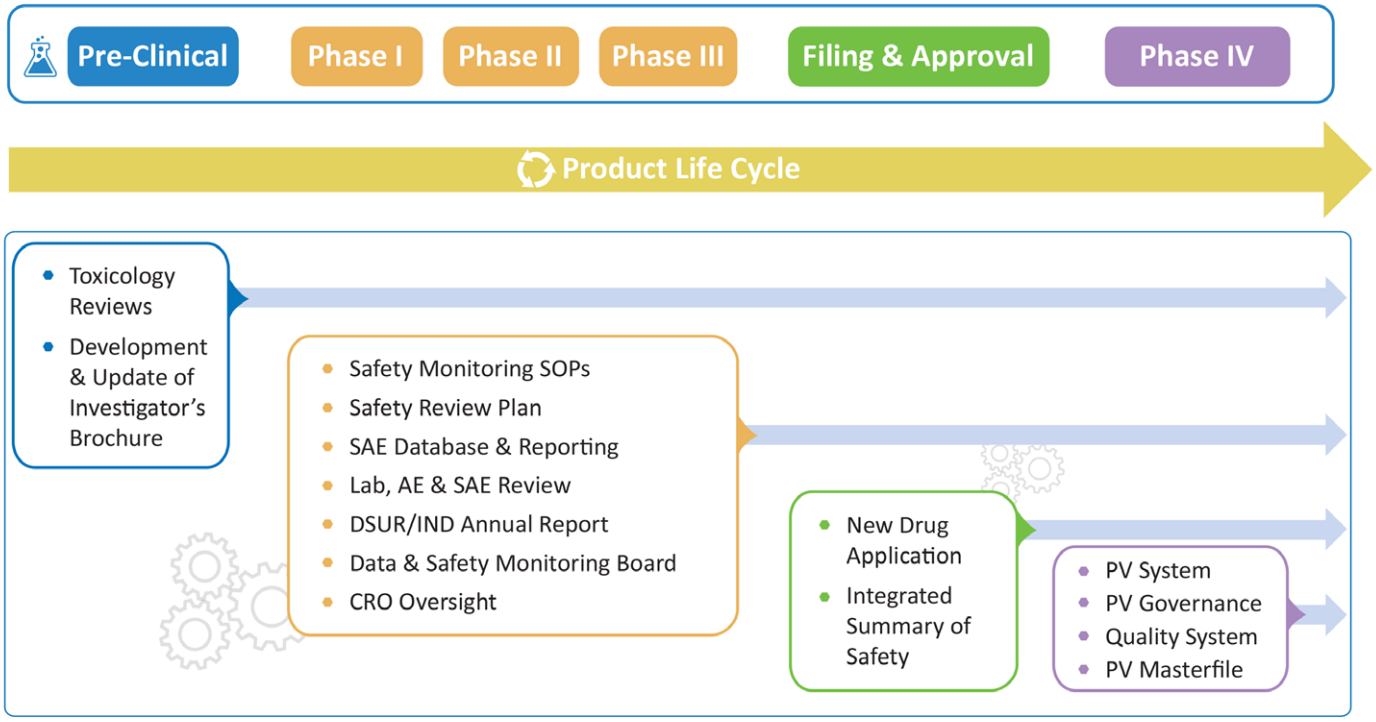
SMEs can benefit by embracing newer strategies to manage their responsibilities during clinical development and in the post-approval phase. Using niche functional service providers (FSPs) that specialize in areas of statistical design and analysis, clinical data management and PV, while using the best-fit CROs to optimize patient recruitment and manage clinical trial conduct ensures the best strategy is implemented.

Common Regulatory and Safety Related Pitfalls during the Product Lifecycle

Figure 1 depicts several critical safety and regulatory related activities that are part of the product lifecycle, from preclinical development through Phase IV. However, smaller organizations are often unable to prioritize these activities and may not have the expertise or resources to undertake all activities themselves. These companies typically have a small team that is responsible for all of the clinical, safety and regulatory activities. Not having distinct and specialized teams often impacts the appropriate prioritization of the various critical activities.

Compliance to safety regulations is of the utmost importance. Regulatory compliance may be compromised if appropriate standard operating procedures (SOPs) and safety management practices are not in place. Suboptimal processes and non-compliance issues can in turn lead to higher costs, through missed work, rework or low quality output[1]. Regulatory authorities such as the US FDA and MHRA issue warning letters for major regulatory violations observed during inspections. Consequences of the warning letters are serious (e.g., loss of trust by patients and HCPs regarding company products, damaging effect on stock prices, and negative impact on approval of future submissions.) The FDA's enforcement actions can include product recall, seizure, injunction, administrative detention and civil money penalties and/or prosecution.

Figure 1: Critical Safety and Regulatory Activities during the Product Lifecycle



The most common pitfalls in safety monitoring during the product lifecycle include failure to:

- Integrate multiple safety databases, required for comprehensive safety review
- Develop robust written SOPs and work instructions for safety management
- Analyze, review and document all pertinent clinical safety data (adverse events and events of interest, laboratory data and other investigations)
- Review and update Investigator's Brochure (IB) on a timely basis
- Coordinate case submissions to regulators, ethics committees and investigator sites across multiple clinical studies, as required and within timelines
- Submit DSUR/IND Annual Reports per schedule and applicable regulations
- Ensure audit and inspection readiness at all times

Similarly, design, analysis and reporting of clinical trials may not be of the desired quality and may cause inordinate delays in submissions even if the patient recruitment timelines are met. This would have serious resource implications for the smaller companies.

Outsourcing – Key Decision Drivers

There are three key areas of consideration which determine and drive an organization's decision process to outsource clinical, safety and regulatory activities: namely people, process and technology (Figure 2).

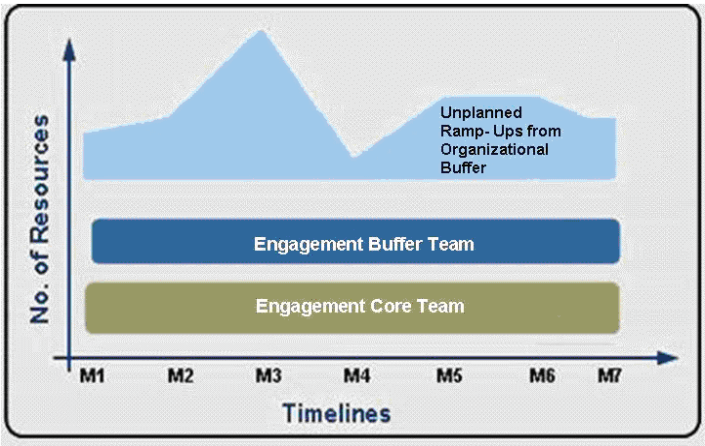
Figure 2: Key Considerations for outsourcing clinical, safety and regulatory activities

The People Factor

Work force limitations with respect to cost and flexibility are an important consideration for SMEs, and external vendors can provide a flexible flow of qualified, competent and specialized personnel. Expertise across distinct work streams including safety, medical, clinical, biometrics, regulatory and technology can be easily leveraged to get the full range of expertise necessary for meeting expected quality standards and regulatory compliance. All of this is possible without the need for the companies to themselves recruit, train and retain dedicated staff.

Spikes and boluses (both planned and unplanned) are a reality in pharmacovigilance, especially of marketed products, and companies need to be ready with a plethora of options to handle different types of spikes (of varying intensity and duration), as seen in figure 3. Working with an outsourcing partner allows convenient access to a broader pool of staff within the outsourcing organization. Resources can be trained and deployed within weeks to manage the increased workload (planned as well as unplanned volume surges/bolus) and can then be withdrawn as needed, providing flexible and cost-effective resourcing solutions for surge management.

Figure 3: Companies need to be prepared for planned and unplanned spikes and boluses



The Process Factor

Developing the right processes to support end-to-end clinical development, regulatory and pharmacovigilance activities is both very costly and laborious. Specialty outsourcing organizations can provide ready-to-go, robust, tested and audited systems and procedures, eliminating the time and expense of starting from square one. These processes can be configured to the company products, processes, and requirements. Further, these processes are updated on an ongoing basis to adapt to changing regulatory requirements and technological advances.

The Technology Factor

Information technology is essential to enabling a robust safety and risk management operation and outsourcing vendors are able to provide ready-to-go infrastructure and technology services, and knowledgeable and experienced technology staff. This also ensures strong business continuity and disaster recovery plans.

Specialized vendors employ best in class quality systems and oversight with well-defined quality management plans, robust SLA compliance frameworks, and metrics, analytics and reporting. Such vendors can help build pragmatic and compliant systems to meet company requirements and development plans.

Advantages & Benefits of Specialized Safety and Regulatory Solutions

In the area of safety and risk management, PV-in-a-Box (Figure 4) is a holistic customer-centric approach that brings together safety, technology and advisory services towards the provision of a complete end-to-end PV solution by a single vendor for the sponsor company. This integrated, flexible and shared services outsourcing model ensures regulatory compliance, quality data, product safety, lower risks, cost savings and allows the sponsor to focus on what they do best – develop and deliver new medicines to the market.

The effective combination of domain expertise, agile processes and robust technology results in high quality and compliant operations, increased efficiency and time savings. At the product level, PV-in-a-Box allows real-time tracking of benefit-risk profile and enables quicker and more informed decisions on risk minimization, ultimately supporting maintenance of efficacious and safer medicines in the market. An automated technology platform (as part of the PV-in-a-Box solution) plays a key role in effective PV management by fostering collaboration between disparate teams, enabling seamless processes and effective analysis of safety data.

Figure 4: PV-in-a-Box is an integrated Regulatory and PV shared services model, encompassing end-to-end activities from safety database implementation, to case processing and medical review, to safety surveillance and risk management. It may include additional services such as QPPV provision (for products marketed in Europe), and call center capabilities.

Efficient study designs and the right analysis and reporting can significantly enhance the success rate of clinical trials. Similarly teams that specialize in market access strategies, and have an understanding of the regulatory environment in various markets, can advise on the submission requirements for regulatory approvals, especially in semi-regulated or non-regulated markets. Such specialized clinical and regulatory support will increase the chances of successful clinical development programs and ultimately of the commercial success of the products.

Conclusion

Both clinical trials and post-marketing activities for medical products continue to grow in complexity and scope. Furthermore, in this constantly evolving and more stringent regulatory environment the task of managing trials is more demanding than ever. With this in mind it is interesting to note that while most of the industry's risk management efforts have focused on post-marketing drug safety, the clinical trial process holds a broad array of other potential risks that could jeopardize a company's product development investment, including regulatory delays.

A common challenge across small and medium sized life science companies is how to create, develop and implement an effective Clinical, Safety and Regulatory operations that can scale and ensure regulatory compliance for their growing product portfolio. Some companies need advice and direction to get their operations started, while others who have processes in place may need help selecting and maintaining technology (e.g., safety database) and services (e.g., medical call center) to centralize and automate their operations.

In addition, regulatory obligations and imperatives span a wide array of areas including clinical development, regulatory submissions and approvals, marketing decisions and product launches across geographies. All of these require a breadth of experience that can be realized only through professionals who specialize in individual areas. It is not practical for small to mid-sized companies to have all the required expertise and experience in-house. It's also not possible for many niche CROs to have the quality of experience across all these areas.

framework and ensuring that processes and SOPs are always compliant is challenging, given an organization's limited resources. The requirement for a Safety Assessment Committee (SAC) in the recent draft guidance for IND safety reporting is a case in point. Aggregate review in real time by an independent team is critical, for which it's important to have all the safety data consolidated in a single database. This has implications on a company's strategy to source safety services right from the early clinical development stage. Another challenge in the safety area is balancing high quality AE processing and reporting against unpredictable volumes while meeting new needs in signaling, surveillance, and risk management.

Smart outsourcing and quality services are dependent on effective business (scientific) processes, well-defined governance structure and long term commitment to continuous improvement. Partnering with a provider who offers a scalable and agile solution with a suite of integrated products such as Sciformix's specialized and customized clinical development and regulatory solutions will go a long way in enabling sponsor companies to stay ahead of the curve. This strategy will help organizations achieve commercial success, get products to patients faster, remain compliant with regulatory requirements, while being focused on patient safety and optimal benefit-risk evaluation of their products at all times.

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References

1. Deloitte. Pharmacovigilance (PV) outsourcing – Emerging PV business models. 2014. (Internet) available at: https://www2.deloitte.com/content/dam/Deloitte/us/Documents/life-sciences-health-care/us-lshc-pharmacovigilance-outsourcing-021115.pdf [accessed 23/01/2017]
2. European Medicines Agency. Guideline on good Pharmacovigilance practices (GPV). (internet) http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/08/WC500211728.pdf [accessed 24/01/2017]

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Sciformix Corporation is a global scientific process organization (SPO) that partners with life science companies to develop, launch and sustain medical products that aim to improve the quality of healthcare worldwide.

We collaborate with our clients through the entire product development lifecycle to provide a full range of services from study design to post marketing surveillance and commercialization support.