



Pharmacovigilance: A Practical Approach to Reshaping Patient Safety

Executive Summary

Ensuring the safety and efficacy of pharmaceuticals and biotechnology products is one of the top challenges in healthcare today. With drug recalls continuing to make headlines, consumers and other stakeholders across the healthcare ecosystem are demanding more oversight and regulators around the globe are responding to these pressures by increasing their scrutiny and compliance requirements from the industry.

Despite the heightened focus on drug safety and the direct link between reactive safety and numerous risks to business – financial, regulatory, brand loss, etc. – many biopharmaceutical companies today still have inefficient drug safety operations and detect safety signals with suboptimal latency. Inefficiencies and redundancies in pharmacovigilance operations result in higher costs and undermine efforts to significantly increase overall performance.

As the pharmaceutical, biotechnology and medical device industries renew their focus on becoming lean and more effective in bringing safer, newer products and therapeutic value to patients in a timely manner, they must transform their drug safety operations. Proactive pharmacovigilance – enabled by globally integrated process, people and technologies – can help the industry achieve its objectives. This can be accomplished by:

- Rigorous analysis, interpretation and “real-time” decision making on safety signals and proactive remediation.
- Leveraging pre- and post-marketing safety patterns and insights for clinical trial design and safety analysis to balance the risk-to-benefit ratio of new products, therapeutic directions and early “go, no-go” decisions advancing drug candidates.
- Allowing for convergence of the evolving regulatory environment and the integrated PV/safety operations and analytics into a source of innovation and competitive advantage.

This paper will examine the key challenges faced by the industry, some of the practical approaches to overcome these challenges and tangible benefits that can be realized in implementing proactive pharmacovigilance as a business strategy.

Global Drug Safety: Key Challenges and Solution Approaches

Based on our experience helping biopharma companies with thorny PV challenges, we recommend the following.

- **Establish a safety and compliance culture.** Until recently, many companies have adopted a piecemeal approach to managing safety and compliance. What is required, however, is a holistic vision and approach – one that guides the whole company towards a culture

of compliance – that allows the staff to understand that compliance makes good business sense. Such a cultural change cannot be brought to bear overnight and will need to be implemented in a phased but timely manner.

- Establish the “safety first” vision and re-emphasize the need for proactive safety and compliance, RiskMAPs and benefits that can be realized with the entire team – both internal and partners – through structured governance/communications from executive and senior management.
- Ensure safety risk assessment as part of

business risk management that is tracked and monitored for proactive remediation.

- Make informed and early decisions on “go, no-go” on products in the pipeline based on signals/safety analytics from launched products and products in advanced clinical studies.
- Implement specific actions and programs that are focused on “getting it right the first time” to avoid intensive/overtime fire-fighting work and costs.

Case Study >>

Proactive Pharmacovigilance

Business Situation: A biopharmaceutical company’s global safety organization wanted to close its cases within a business day, regardless of the time or locale of origination. Cases were sometimes backing up because of holidays, time differences and vacations and lack of available staff (capacity).

Challenge: Achieving the 24-hour resolution goal apparently would require the company to invest in new call centers, case processors and medical reviewers around the globe as well as virtual tools and workflow technologies and dashboards/portals. The centers would be expensive to set up, staff and operate.

Solution: The company elected instead to work with us to adopt an outcome-based service

delivery model. Cases are processed around the clock, around the world, with virtual teams of globally-based experts and operational teams sharing data.

Benefits: In collaboration with the client, we are developing a globally integrated and networked model of operating centers that are governed by a single leadership team and a set of innovative systems/tools. We are taking accountability for delivering the cases in a timely manner with increased quality and reduced cost of operations across a scope of activities including case booking, processing, medical review and closure. Because of our participation in global clinical data management, we also can provide insights to help the client to anticipate potential issues.

A Better Approach to PV

Here is how we collaborate with this client to make PV more proactive.

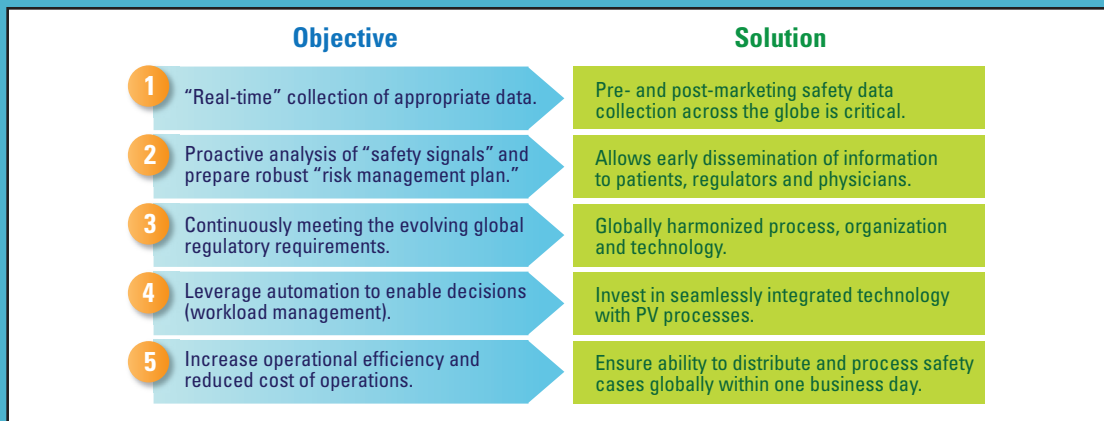


Figure 1

- **Develop/refine capabilities to manage regulatory changes in “real-time.”** Regulators across the globe have varying and continually changing reporting requirements. To operate globally, life sciences companies must meet these requirements as well as local timelines, reporting formats and translation requirements.
 - A critical activity is keeping abreast of regional regulatory changes for registration and reporting. Life sciences companies need a dedicated group of analysts and regulatory experts who follow evolving trends and provide guidance on class-wide Risk Evaluation and Mitigation Strategies (REMS), alignment between global regulatory agencies (ICH, EU, FDA, Japan, etc.), post-marketing data collection, integration and analysis, guidance on training, policies and reporting to all stakeholders.
- **Implement globally aligned processes, technology and governance.**
- **Processes.** To gather comprehensive data, life sciences companies must manage global drug safety operations and coordination of case processing through a “single harmonized process” with options for local customization to fit regulatory requirements. These include:
 - A seamless operating model that integrates case processing volumes, types and submissions timelines (“demand”) with a globally flexible and scalable resourcing (“capacity”) model, across the sponsor and the global partners/service providers.
 - Identifying drug risk profiles using pre-clinical and relevant post-marketing data (e.g., population diversity and sample size) before future clinical trials are designed.
 - Following up with subjects after completion of trials and analysis of adverse-event-related patient withdrawals.
 - Ensuring that comprehensive post-marketing process including regular case handling, reporting, labelling changes and active querying.
 - Signal generation, evaluation, adequate trend analysis, documentation, disposition and archival.
 - Assessment and review of risk/benefit analysis in the context of evolving risk-based understanding.
- **Technology.** Many global life sciences enterprises find that drug safety data is collected in silos owned by different departments. Correlating data and signals amongst these usually incompatible systems with their lack of standardized data is often a labor-intensive, slow process at odds with today’s real-time orientation.
 - Develop a centralized database that can integrate disparate data and information from different sources internally, third parties and physicians.
 - Ensure the ability to draw PV information/insights from case report forms (CRFs) on a “real-time” basis, which may have significant value on managing risks.
 - Implement best practice global work flow, analytical tools and dashboards for real-time insights and decision making.
- **People/capability improvement.** Focusing core professional staff on mission-critical activities will have a direct impact on cost and efficiency and the ability to move towards “proactive patient safety.” Retaining core/strategic activities internally while leveraging global partners to provide transactional/operational case handling processes more efficiently at high quality can allow for a robust people strategy.
 - **Typical internal activities include:**
 - Regulatory interface/submissions related, policies and reviews.
 - Risk management/integrated epidemiological and statistical analysis, risk communication and education systems and translation of pre-clinical data.
 - Signal detection/reporting: REMS and processes, complex periodic reports and integrated review of all emerging signals.
 - **Typical external, global partners-driven activities include:**
 - Best practice adverse event intake and harmonized processing that will allow for continuous productivity improvements.

Life sciences companies need a comprehensive people capability review that includes their own expertise as well as complementing partners' expertise that allows for a flexible and scalable staffing model with the right skills that can adhere to their “proactive patient safety” vision.

- Global safety database management and support.
- Global aggregate reporting/PSUR process.
- Report templates/-authoring tools.
- Medical review and narrative writing.

Life sciences companies need a comprehensive people capability review that includes their own expertise as well as complementing partners' expertise that allows for a flexible and scalable staffing model with the right skills that can adhere to their "proactive patient safety" vision. This will also allow management of case volume fluctuations by location and therapeutic class.

- **Structured governance.** Leading life sciences companies are making a fundamental shift to moving drug safety and clinical development into a single functional team that has the mandate and authority to define and enact integrated clinical and drug safety policies and processes throughout the enterprise (IT, packaging, clinical operations, quality assurance and biostatistics) and with partners. This means they must:
 - > Implement a streamlined governance structure that encompasses internal teams, collaborators and partners around the world with clearly identified forums, participants (RACI) and a robust communication plan.
 - > Identify and empower a small data standardization unit to continuously develop and manage the overall safety processes, tools and data standards to ensure that policies, new process changes and tools are only implemented in compliance with these standards.

The Rewards/Benefits of Proactive Pharmacovigilance

Developing an integrated and reshaped patient safety organization can provide significant benefits. These include the following:

- **Reduced total cost of ownership.** Having uniform, global processes, systems and governance will allow efficient data and information capture, analysis and real-time decision making that can directly lead to reduced cost of operations by >30% that is a combination

of continuous productivity improvements, synergies between case processing and IT automation/work flow technologies, globally shared governance and oversight that a partner can leverage.

- **Continuous improvement, innovation and transformation.** Applying Lean and Six Sigma principles along with customized quality management plans (QMP) can lead to measurable productivity improvements across case-handling processes (e.g., data entry, coding). Selected initiatives and benefits from such efforts include:
 - > Improving the accuracy of data entry and coding by 10% to 15%.
 - > Improving the accuracy of narratives by 30%.
 - > Reducing the processing time for cases by 20% to 50%, per case type.
 - > Reducing time to write narratives by 60%.
- **More collaboration and better compliance.** Life sciences companies with global pharmacovigilance operations will be able to participate more effectively in collaborative efforts with partners, academic organizations and regulatory bodies on such efforts as REMS and address international regulatory initiatives on a proactive/reactive basis.
- **Smarter R&D decision making allowing for safety as a competitive asset.** Proactive pharmacovigilance also enables life sciences enterprises to make better decisions about current and planned research and development activities. They can correlate incoming post-market and trial signals data to related product and therapy development. Such correlations may indicate a planned trial should be redesigned or that an effort should be ended because it appears unlikely to garner satisfactory trial results. Data may also indicate where ancillary development efforts could benefit another patient population.

Moving Forward

Approaching pharmacovigilance as an enterprise-wide business strategy still is not the norm but is quickly becoming so. Life sciences companies that embrace this shift will be able to meet near-term demands for drug safety assurances from a range of global stakeholders. Most approved products are subjected to risk mitigation plans of some sort. Simultaneously, life sciences companies are

staking out a competitive advantage in the form of more and better data, used intelligently to help evaluate and direct future clinical development and for post-marketing evaluation of comparator products. The net impact will be that life sciences

companies will be in a better position to deliver the higher quality, lower cost products the market requires and deliver ultimately better quality of life to patients.

About the Author

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