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Challenges in Global Pharmacovigilance

- Addressing these challenges using effective tools

by Sharad V Deshpande
Associate Director, Product Marketing



Executive Summary:

Today's increasing pace of innovation in the Life-Sciences industry is resulting in ever larger number of drugs and medical devices coming to the market every year. Simultaneously, geographical expansion into newer markets has resulted in exponential business growth. Despite the continued work during the past few decades towards harmonization of regulations across various ICH regions, the fact remains that there are wide differences in regulatory bodies and the respective regulations they mandate on life sciences companies functioning in their ambit. The developed economies have well established regulatory oversight bodies (like the FDA, EMA and PMDA) that have laid out clear Pharmacovigilance functioning and reporting requirements. Many of the developing regions on the other hand are evolving their national regulators as well as their respective regulations. This scenario of sustained business growth and diverse, evolving regulatory requirements to comply with across regions poses several unique challenges to the pharmacovigilance departments in these companies.

In order to successfully function across multiple markets, life sciences companies must evolve their internal processes and systems to comply with diverse regulations effectively. Many organizations continuously optimize their pharmacovigilance practices in response to evolving market and regulatory requirements. Several organizations have completely outsourced their entire pharmacovigilance functions to dedicated service providers in anticipation of being able to benefit from economies of scale that vendors promise. Whatever be the case, the Pharmacovigilance departments today face several unique challenges. This paper will delve into some of these challenges and how they affect multiple roles within the pharmacovigilance and safety departments of life sciences organizations. It will also discuss how giving due consideration to certain specific factors will help pharmacovigilance departments to successfully meet their business expectations for now and for the future.



Importance of Pharmacovigilance systems

Current Scenario:

Pharmacovigilance departments face continuous challenges in keeping up with business growth and evolving regulations. Some of these challenges are strategic while others are operational in nature and affect daily operations. They have significant impact across all key departmental roles – from the Head of Pharmacovigilance, QPPV, PV Operations Managers, case processing staff to the IT staff and managers maintaining pharmacovigilance business applications and associated infrastructure. A comprehensive view and an understanding of all the issues faced in each of the departmental roles will significantly help craft an effective evolutionary roadmap for the Pharmacovigilance departmental processes and systems.

Pharmacovigilance departments are broadly responsible for:

- Sustaining compliance with continuously evolving regulations and maintaining effective vigilance and reporting across pre and post-marketing phases of drug and device development.
- Effectively managing pharmacovigilance in the midst of constant business changes occurring due to acquisitions, mergers, business growth into newer markets, etc.
- Ensuring compliance with regulations of multiple regulatory authorities across different geographies
- Effective adoption of newer requirements like signal detection and management to ensure early and accurate benefit-risk profiling for all products
- Ensuring cost effective and efficient operations on a global scale

To successfully meet these business requirements effectively, pharmacovigilance teams need to:

- Continuously deliver multiple statutorily mandated reports – Expedited and Periodic.
- Maintain high levels of data quality and privacy.
- Maximize paperless processes as much as possible.
- Ensure seamless transfer of data across multiple siloed applications.
- Sustain application infrastructure availability, performance, and scalability to meet business requirements.
- Manage vendor relationships effectively to ensure critical issues are addressed in a timely manner.

Typical Pharmacovigilance Roles and their unique challenges:

A typical Pharmacovigilance department is structured with roles as laid out in the chart below.

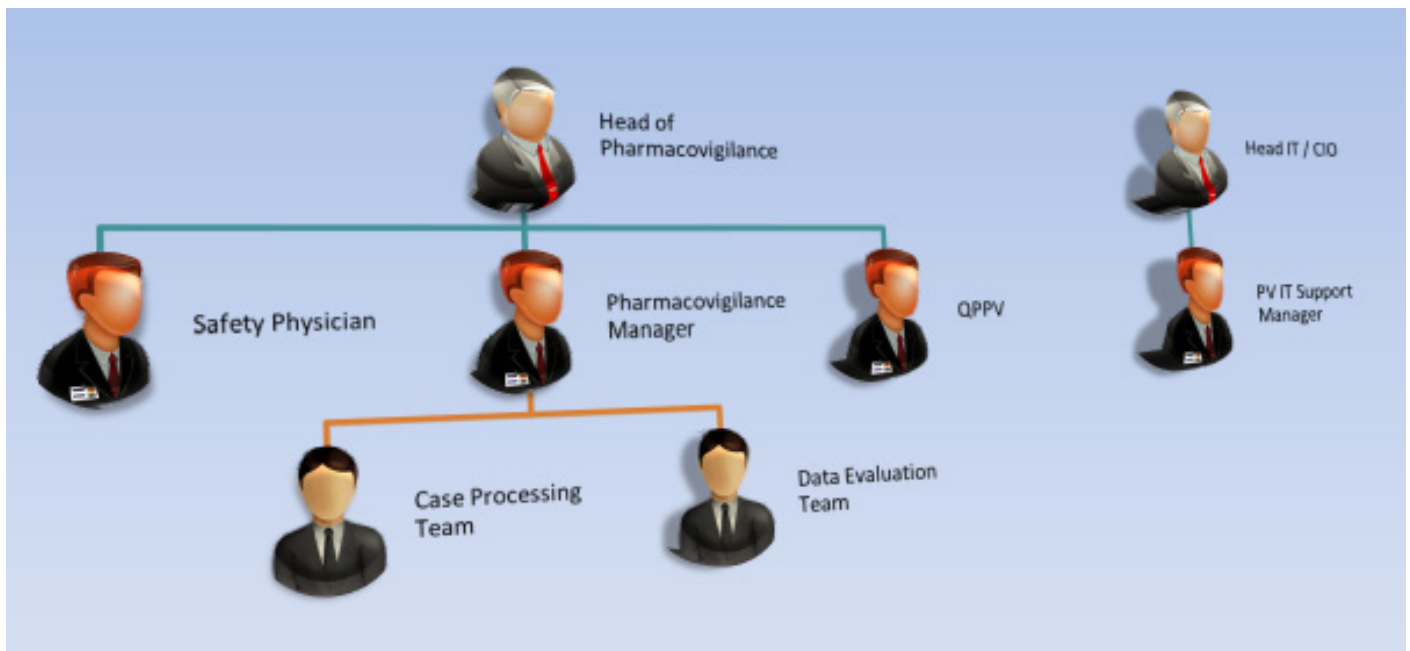


Figure 1: Organization structure of a typical Pharmacovigilance department

Let's take a closer look at a few of the key roles, responsibilities, challenges, reasons why these challenges exist, their impact on business and how to effectively manage them.

Head of Pharmacovigilance



Key Responsibilities: Oversee and direct all key Pharmacovigilance activities such as (but not limited to): data collection, evaluation and submission of Individual Case Safety Reports (ICSR), preparation and submission of Periodic Safety Update Reports (PSUR), risk management, signal management, Pharmacovigilance Master Files, and transmission and reconciliation of data. Besides these operational activities, the role is also responsible for ensuring compliance with relevant legislation across all operating markets. On the organizational side, the role is responsible to ensure all departmental staff is appropriately trained and systems and processes are sufficiently well laid out to meet the organizations business requirements.

Head of Pharmacovigilance – Challenges & Considerations

Continuously evolving regulations and business processes

- Applications configurability to accommodate changes in business process and reduce maintenance requirements

Necessity to maintain compliance at national and international levels

- System should support management of safety reporting in accordance with international standards and guidelines

Efficient and cost effective operations across all markets

- Cloud based applications can significantly help in reducing the overall cost of ownership by reducing direct investments in hardware, software and supporting IT staff

Key Challenges and Considerations: A few of the key challenges faced by the Head of pharmacovigilance include:

1. Challenge - Continuously evolving regulations and business processes:

The regulatory environment is increasingly demanding and is a global phenomenon. Compliance with latest regulations such as the E2B (R3), and IDMP are in various stages of being mandated across various ICH regions. Business growth into newer markets necessitate that the PV systems and processes scale smoothly and sufficiently. Ensuring that existing Pharmacovigilance systems and applications constantly evolve to support the business effectively is a significant requirement. These evolving regulations impact PV operations at multiple levels and many have fundamental implications for the underlying database structure, configurability, reporting capability and integration with other systems and data sources. Inadequate support for new and evolving regulations can result in potential regulatory non-compliance and associated penalties. In addition, reporting in the non-ICH regions is even more challenging as the requirements vary more widely than among ICH countries.

Consideration: Effective management of this challenge requires design, development and roll out of efficient and cost-effective clinical safety and pharmacovigilance programs. While the business processes can be structured fairly easily, the underlying PV application and its associated infrastructure can quickly become bottlenecks requiring extensive customization, implementation and integration. All these can easily drain the departments IT resources and budgets. Hence, while planning for the PV applications (either extending an existing one or implementing a new system), sufficient consideration should be given to the applications configurability to accommodate changes in business process and reduce maintenance requirements. Additionally, the system should support management of safety reporting in accordance with international standards and guidelines “out of the box”. PV solutions that are available on the Cloud can also significantly help in reducing the overall cost of ownership by reducing direct investments in hardware, software, and supporting IT staff. A good service provider can provide significant benefits from economies of scale and deliver systems that are constantly upgraded to ensure compliance with the latest evolving regulations across ICH regions and beyond.

2. Challenge - Necessity to maintain compliance at national and international levels:

Regulatory reporting requirements across countries can require manual workarounds/process interventions creating significant room for error and increase risk. Different regulatory reporting requirements for post marketing and clinical trial stages also have the potential to cause significant increase in workload and supervision. Without a global PV system, the demands and workload of local PV teams increase significantly, resulting in increased risks and reduced productivity leading to inefficiencies. Local PV teams face challenges in submitting cases as per local regulatory requirements in a timely manner.

Consideration: In order to maintain compliance globally, PV departments should consider using comprehensive solutions that can help eliminate redundant data entry and automate the many case-processing functions involving data exchange facilitation by ICSR between headquarters and local affiliates across multiple ICH regions. The solution should provide one underlying application with multi-language support, which is compliant with international regulations – United States, Japan, and Europe and beyond while providing improved efficiencies regarding data entry and validation.

3. Challenge - Efficient and cost effective operations across all markets:

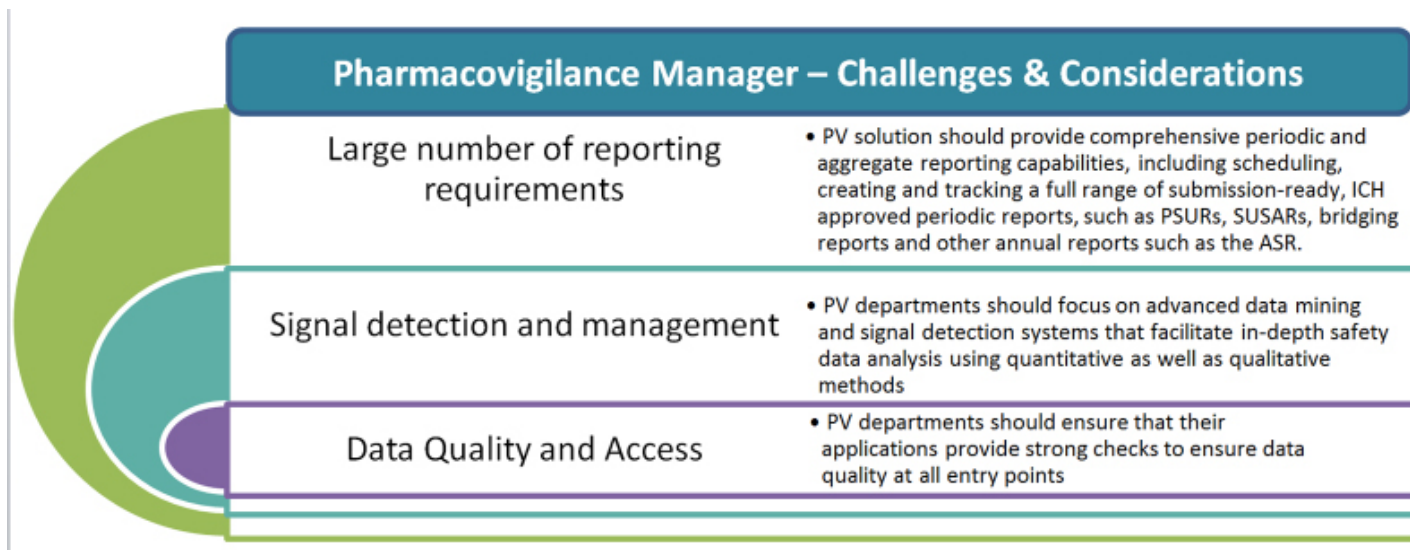
Sending and submitting cases across ICH regions presents a significant challenge for an organization. Some companies send their data by fax or as PDF files in an email to subsidiary companies that re-type the data into local systems and create the Individual Case Safety Report (ICSR) for the local regulatory authorities. A few companies also send the submission data back to headquarters so the central system can be updated. Thus, the lack of automation leads to manual routing and tracking of cases and can cause process bottlenecks resulting in inefficient processing of AEs and reports.

Consideration: PV departments should consider single, centralized solutions where possible. Such solutions provide a single global view of safety issues enabling worldwide pharmacovigilance programs. The solution should provide multi-lingual support and should be constantly updated by the vendor to ensure that the system complies with the latest regulations across ICH regions. Solutions providing configurable case processing workflows enable companies to deploy international workflows from a single global database for consistent case processing and reporting procedures. With an integrated solution and single database, the system is installed, configured, and validated only once. Companies can realize tremendous cost savings when licensing a single database and performing subsequent upgrades.

Pharmacovigilance Manager



Key Responsibilities: Manage the pharmacovigilance team to ensure work is distributed, planned effectively and training is organized as appropriate. Manage all key pharmacovigilance activities such as (but not limited to): data collection, evaluation and submission of Individual Case Safety Reports (ICSR), preparation and submission of Periodic Safety Update Reports (PSUR), Risk management, signal management, Pharmacovigilance Master Files and transmission and reconciliation of data.



Key Challenges and Considerations: A few of the key challenges faced by the pharmacovigilance manager include:

1. Challenge - Large number of reporting requirements:

Periodic reports are a practical and achievable mechanism for summarizing interval safety data, especially covering short periods (e.g., 6 months or 1 year), and for conducting an overall safety evaluation. In addition to covering continuing safety issues, periodic reports should also include updates on emerging and/or urgent safety issues, and major signal detection and evaluation events that are addressed in other documents. Periodic reports — PSURs, ASRs, and IND reports and DSURs — not only help to ensure that regulatory requirements are met in a timely manner, they also provide the opportunity to document a product's safety profile as it changes over time. Untimely delivery or missed delivery of management metrics, periodic reports, special-purpose reports, or statistical analysis can result in regulatory notification, audits, and associated penalties.

Consideration: The PV solution deployed should provide comprehensive periodic and aggregate reporting capabilities, including scheduling, creating and tracking a full range of submission-ready, ICH approved periodic reports, such as PSURs, SUSARs, bridging reports and other annual reports such as the ASR. The system should allow authorized users to perform detailed analyses of safety data within the specified reporting period and support the assessments provided.

2. Challenge – Signal detection and management:

Given the ever-increasing volumes of the adverse event data, it is very difficult for the reviewers to rely on qualitative methods alone to monitor, detect and manage all possible emerging trends. Manual processes are time consuming; it might take a reviewer a couple of weeks to analyze a signal. Query and response cycles between regulators and life sciences companies are rapidly shortening and reviewers need to analyze signals quickly, typically in a matter of a few days. It is also important that the reviewers are able to focus on real issues and decrease the time and effort spent in analyzing false signals. Therefore, advanced signal detection and management tools are needed to allow researchers to detect and interpret both existing and new types of safety-related data more efficiently. Inefficient signal detection and management leading to inability to comply with regulatory reporting requirements can result in audits and penalties.

Consideration: PV departments should focus on advanced data mining and signal detection systems that facilitate in-depth safety data analysis using quantitative as well as qualitative methods. The system should incorporate all relevant data sources to help companies better understand the benefit-risk ratio of products and allow reviewers to record and track their opinions and analyses. It should allow users to analyze any potential signals using its integrated data mining capabilities and then assign confirmed signals to the workflow for further review and analysis. It should also enable users to perform multi-level drill down into datasets or subsets of datasets to examine the profile of each product using patient demographic, drug and hierarchy data.

3. Challenge – Data Quality and Access:

Over time there has been an escalation in the volume and type of data collected during the life cycle of the product, resulting in an increase in the complexity and diversity of the systems in which this information is captured and stored. There are two reasons for assuring data quality. First, identifying data must be present for a case to exist, and second, sufficient data must be available to analyze the situation. Furthermore, the current landscape has evolved in to a globalized and highly decentralized environment, challenging existing systems, data storage, monitoring and auditing. Companies must develop reliable, proactive and easy follow-up systems.

For aggregate reports and signal detection, data entry and data coding standards are vitally important. Even if this wasn't true in the past, remedial efforts will be required to correct historically poorly coded data, and software checks will be required to maintain quality for newly entered or acquired data. Product definition data needs to be regulatorily up-to-date, not only at present but also as-at any point in history. These are very unique challenges and the PV applications and systems should be able to cater to these specific requirements or else errors in aggregate reporting, incorrect signal detection and regulatorily invalid information being recorded can easily become a reality.

Consideration: PV departments should ensure that their applications provide strong checks to ensure data quality at all entry points. The system should enable centralized enforcement of data quality checking rules to be rolled out across the entire department. Further, the systems should provide an adequate level of data security and privacy. The system should support a centralized coding function that requires more sophisticated coding capabilities to allow the coding group to quickly provide accurate and consistent terms. It should further support term coding using advanced algorithms such as phonetic searching, fuzzy logic and also support an impact analysis where versions of MedDRA can be compared.

QPPV



Key Responsibilities: The QPPV is responsible for establishing and maintaining the pharmacovigilance system and ensuring that information regarding all reported suspected adverse reactions is collected and collated in order to be accessible at least one point within the community. The QPPV is responsible for overseeing the safety profiles and any emerging safety concerns in relation to all medicinal products marketed by the organization. The QPPV acts as a single contact point for competent authorities on a 24-hour basis. The QPPV must have oversight of the pharmacovigilance system in all relevant aspects, including quality control and assurance procedures and compliance reports. The QPPV is responsible for ensuring that a system is set up for regular audits. The QPPV will attend regulatory inspections.

QPPV – Challenges & Considerations	
Quality control and assurance procedures	<ul style="list-style-type: none"> • A global, single pharmacovigilance solution will significantly help in providing the necessary updated views and assessments of risk profiles of products in real time
Maintain Compliance	<ul style="list-style-type: none"> • Systems should provide capabilities that allow for enforcing quality checks globally to ensure data quality & privacy, high levels of configurability that allow for quick extension and deployment of pharmacovigilance processes to newer markets
Manage global benefit-risk profile across entire product portfolio	<ul style="list-style-type: none"> • System should provide all the necessary capabilities for effective data capture across multiple channels, electronic submission to various authorities globally and supports audits


Key Challenges and Considerations: To a large extent, the challenges faced by QPPV are mostly the same as the strategic challenges faced by the Head of Pharmacovigilance. The QPPV needs to have a comprehensive global overview of the risk-profile of all products – which would require complete visibility into the global pharmacovigilance programs. Early and effective signal detection and management is another key expectation of the QPPV as well. All these are in addition to ensuring that the business is compliant with statutory regulations at all times.

Consideration: The strategic challenges facing the QPPV need to be addressed along the same lines as those of the Head of Pharmacovigilance. A global, single pharmacovigilance solution will significantly help in providing the necessary updated views and assessments of risk profiles of products in real time. At the same time, systems that provide capabilities that allow for enforcing quality checks globally on ensure data quality and privacy, high levels of configurability that allow for quick extension and deployment of pharmacovigilance processes to newer markets will significantly help the QPPV. Another important consideration from a QPPV perspective is to ensure that the system also provides all the necessary capabilities for effective data capture across multiple channels, electronic submission to various authorities globally and supports audits.

Head of Information Technology Support / Pharmacovigilance IT support Manager



Key Responsibilities: Many organizations typically have a focussed IT support manager responsible for ensuring all IT requirements from the PV department are delivered as per their SLAs. This role may functionally report into the Head of IT/CIO at the corporate level. The PV IT Support Manager would be responsible for ensuring that the Pharmacovigilance applications used by the department are always available and meet business user expectations. The applications and systems should seamlessly integrate, work with each other and scale sufficiently to meet business growth. Whenever the application vendor publishes any new upgrades or patches, the IT support Manager is responsible for ensuring that these are rolled out to the PV department efficiently without disrupting operations. Simultaneously, the IT support manager is responsible for ensuring that any new requirements coming from the business users are collated and communicated to the vendor and fixes are delivered by the vendor in a timely manner.



Head of IT Support for PV – Challenges & Considerations	
System Integration	<ul style="list-style-type: none"> • Applications should be flexible to aid reconfiguration and extensible to reduce extensive integrations
Application Reliability, Availability & Scalability	<ul style="list-style-type: none"> • Applications should be robust to ensure reliable performance and scalability
System security & data privacy	<ul style="list-style-type: none"> • Applications should adapt to constant technological evolution to keep up with latest IT standards

Key Challenges and Considerations: Some of the key challenges faced by the PV IT support Managers include issues associated with integration of applications and sharing of data between siloed applications, availability and scalability of applications. Poor scaling and performance leads to system break downs resulting in unavailability of mission critical systems to business users impacting business. Working around a lack of application integration requires manual intervention which can result in data inconsistency causing loss of productivity and inefficiency - which leads to increased workload on IT resources.

Apart from these, many of the legacy systems are typically not up to date with the latest IT technologies and standards. This can result in potential data security and privacy issues, leading to increased time to market and potential compliance issues.

Many a times, support managers also have significant issues in managing vendor relationships, particularly when the vendors are not very responsive. This usually results in a significant portion of the PV department waiting for the vendor to address feature requests and implementing manual workarounds. To overcome pressing business needs, IT support managers are hard put to customize systems using external consultants – resulting in expensive and unmanageable systems.

Consideration: Given the challenges outlined, from an IT support perspective, few of the most important factors to consider in using or developing PV applications would include:

- Application flexibility to aid reconfiguration and extensibility to reduce extensive integrations
- Robustness to ensure reliable performance and scalability
- Constant technological evolution to keep up with the latest IT standards.

Vendors with sufficient credibility and established responsiveness to client needs can go a long way in easing the pressures of PV IT Managers.

Summary :

Pharmacovigilance teams need to continuously evolve their processes and systems to effectively support business growth and ensure compliance. The PV applications need to be chosen with due consideration to the responsibilities and the challenges of various roles in the department. The table below summarizes the challenges faced by these roles and factors to be considered while choosing appropriate applications.

Head of Pharmacovigilance

Key Challenges

- Continuously evolving regulations and business processes
- Necessity to maintain compliance at national and international levels
- Efficient and cost effective operations across all markets

Consideration

- Applications configurability to accommodate changes in business process and reduce maintenance requirements
- System should support management of safety reporting in accordance with international standards and guidelines.
- Cloud based applications can significantly help to reduce the overall cost of ownership by reducing direct investments in hardware, software and supporting IT staff.

Pharmacovigilance Manager

Key Challenges

- Large number of reporting requirements
- Signal detection and management
- Data Quality and Access

Consideration

- PV solution should provide comprehensive periodic and aggregate reporting capabilities, including scheduling, creating and tracking a full range of submission-ready, ICH approved periodic reports, such as PSURs, SUSARs, bridging reports and other annual reports such as the ASR.
- PV departments should focus on advanced data mining and signal detection systems that facilitate in-depth safety data analysis using quantitative as well as qualitative methods.
- PV departments should ensure that their applications provide strong checks to ensure data quality at all entry points.

QPPV

Key Challenges

- Quality control and assurance procedures
- Maintain Compliance
- Manage global benefit-risk profile across entire product portfolio

Consideration

- A global, single pharmacovigilance solution will significantly help in providing the necessary updated views and assessments of risk profiles of products in real time.
- Systems should provide capabilities that allow for enforcing quality checks globally on ensure data quality & privacy, high levels of configurability that allow for quick extension and deployment of pharmacovigilance processes to newer markets
- Systems should provide all the necessary capabilities for effective data capture across multiple channels, electronic submission to various authorities globally and support audits

PV IT Support Manager

Key Challenges

- System Integration
- Application Reliability, Availability & Scalability
- System security & data privacy
- Vendor Responsiveness

Consideration

- Applications should be flexible to aid reconfiguration and extensible to reduce extensive integrations
- Applications should be robust to ensure reliable performance and scalability
- Applications should adapt to constant technological evolution to keep up with the latest IT standards

Conclusion :

Amidst the increasingly regulated and evolving business environment, Pharmacovigilance departments need to weigh multiple factors as they chart out their own roadmaps. Whether organizations decide to develop their PV applications in-house or procure them from a vendor, giving due weightage to each role in the PV team, the unique challenges they face and how they will evolve in the future can go a long way in establishing a sound strategy that serve will eventually serve the business well.

Total Safety™ from ArisGlobal is designed to enhance the functional excellence of life science organizations as it pertains to drug safety reporting and risk management practices. It focuses on those elements over which safety must have full control and meet the demands of pharmacovigilance and risk management for the product portfolio. It empowers the QPPV to deliver premier pharmacovigilance practices on a global basis, manage all pharmacovigilance activities, meet all regulatory obligations and commitments, enhance risk management initiatives, and maintain inspection readiness. The Total Safety suite comprises proven and mature solutions for recognizing operational efficiencies across the enterprise while protecting products from increased regulatory and public scrutiny.

About the Author

Sharad V Deshpande heads Product Marketing at ArisGlobal. He has over 15 years of experience in the Enterprise Software Products industry. Over these years, he has held various roles in conceptualizing, developing and marketing innovative software products to diverse industries such as Life Sciences, Automotive, Aerospace, Finance, Banking and Insurance among others, while working at companies like IBM & Siemens. Prior to ArisGlobal, Sharad was with IBM, managing the development and marketing of IBM's industry leading transaction processing middleware platforms. Sharad received his MBA from University of California, Irvine in 2005 and Bachelor of Technology from Indian Institute of Technology, Madras in 1998.

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