

Drug Safety Grows Up

Increased regulations and worried customers are just two of the factors driving trends in drug safety and risk management today. Examining the present situation, Deborah Gold at WCI Consulting Ltd predicts a new, pro-active pharmacovigilance environment for the future.



Deborah Gold has been a Business Consultant since 1992. Since joining WCI Consulting Ltd in 1998, she has helped a number of global pharmaceutical companies develop effective and efficient pharmacovigilance systems to best meet their current and future needs. Deborah currently runs WCI's PV forums; 'pvnet' and 'pvconnect' – sharing best practice, benchmarking performance, debating common challenges and helping the industry to adopt a more proactive approach to pharmacovigilance.

Heads of Pharmacovigilance (PV) are currently undergoing something of a rites of passage. In the youth of their careers the focus for their Drug Safety (DS) teams was compliance with operational regulations. And it worked. Most Drug Safety teams now have both their compliance and their basic operational processes well under control.

However, times and regulations are changing. The focus of the regulators has expanded to proving that DS teams have a structured approach to mitigating risk in place, and if not, they are ready to strongly enforce the penalties.

Worried consumers, alarmed by media reports of Big Pharma's rumored preference for profits over patient safety, are adding to the call for the industry to take a wider and more pro-active approach to pharmacovigilance. The spotlight on safety is brighter than ever: and PV Heads are now required to take a more holistic view going forward, and find and develop opportunities for building safety into the wider drug development process.

In a way it's good timing. With the operational side well controlled, the maturing PV teams are ready to move their attentions from the operational to the analytical. Since most companies are also resource constrained, they must accomplish increased focus on the expanded drug safety activities without a corresponding increase in total resources. These factors are driving trends in drug safety and risk management, which are both structural and organisational.

Trend 1 – Getting PV involvement earlier in the product life cycle

PV groups are increasingly responsible for safety activities within clinical teams, in early- and late-phase development of drugs and, as discussed, there is a focus on getting Safety Risk Management activities initiated earlier in the product life cycle.

This shift is driven, in part, by impending regulatory changes that will mandate that benefit-risk management must begin in early phase development. It is also consistent, however, with companies'



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migration toward proactive pharmacovigilance, as it affords a more complete view of a product's safety profile throughout its lifecycle.

These issues introduce and reinforce the challenge to appropriately 'skill up' PV resources so that they can establish and maintain their credibility within Clinical. DS need staff who have a deep knowledge of early phase processes and tools, can make convincing Risk Management decisions and can use aggregate data and mining techniques that enable pro-active pharmacovigilance.

At present people with this new skill set are rarities in DS. Going forward PV Heads are looking to build more cross functional teams, developing select staff using physicians with clinical expertise in key roles. They are also looking at building a more robust career path for these individuals that will allow them to move easily between the clinical and safety paths.

Trend 2 – Increase focus on proactive safety surveillance

Recent research into PV Heads' spending has shown a 10% reduction in investment in single case handling. This important move is indicative of a change in approach, with many Heads now altering their way of thinking from 'operationally' to 'organisationally.' PV Heads are evaluating their organisational models, resources and physical locations. For example, many are reducing the number of Data Processor roles and replacing them with multi-skilled Scientists who are capable of doing the analytical activities so important to improving overall safety.

A number of companies have also centralised their geographic centres. With standard ways of working in place on a more manageable number of sites, cases can be put through faster and are available for aggregate review and risk management more quickly and efficiently.

Although ostensibly driven by economic needs, regulatory pressures on Heads of PV and QPs to ensure standards and quality of all outputs are contributing to the 'fortification' instinct. There is recognition that it is easier to ensure consistency and control by operating a smaller number of large case handling and/or data entry centres than a larger number of small ones.

The development of dedicated Support Functions and associated SOPs and Metrics is an enabler for both these organisational changes.

Trend 3 – Gaining increasing confidence in the signal detection processes

Recent research indicates PV Heads are spending 14% more on signal management than in 2005, which indicates increased confidence in signal detection. Many teams are early on in the process and are exploring the use of different techniques and approaches, and as a result we are seeing more signals confirmed and product safety profiles regularly reviewed. This has to be positive news for the industry as it shows an increased focus in this area and a growth in maturity in the way PV teams are analysing the products. We are also beginning to see the creation of 'surveillance engines' with standard review processes and tools and high flow rates producing regularly updated safety profiles.



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However, there are new challenges that come with this increased activity. For example, how can the increased outcomes be appropriately handled? Are our existing methods of documenting rejected signals, reporting confirmed signals, and then putting the label change process through suitable? Are we erring on the side of caution? Is this causing stress to existing processes and Regulatory departments?

This is a fast emerging area where final Volume 9a regulations are still to be published; so another dilemma for PV teams is how to meet requirements effectively whilst waiting for the laws to become established.

Trend 4 – Evaluating their safety databases

Pharmacovigilance systems consist of a drug safety case information database with a set of tools and techniques for mining to detect “safety signals” buried inside the massive data sets. The test for drug companies and the regulators is to leverage these technologies to make better decisions about drug safety, and the challenge for PV Heads today is to find a system that covers their basic operational needs, as well as allowing the aggregate reviewing that enables safety risk management. Many companies are opting to switch or upgrade to a new, customised, off the shelf solution. This has two positives; firstly, teams can buy a system configured to their exact needs and changing requirements, and secondly, if they buy a supported solution by a recognised provider they can leave the maintenance and development to the vendor and get back to focusing on safety.

There are four major vendors who have mature safety database systems – Phase Forwards (Clintrace), Reisis (Argus), Aris Global (ARISg) and Oracle (AERS). These systems enable teams to gather the case information needed and meet current PV regulations. However, there is some way to go before these systems are able to provide the deep analysis and data mining required for truly effective signal detection and risk management; working with vendors on this and balancing their other changes in PV will be a major challenge for DS teams in the near future.

Trend 5 – Building a structured approach to risk into safety

A recent survey of Top 20 Pharma companies found that most companies are reviewing or plan to undertake new approaches with respect to Safety Risk Management. Thus there is a definite need for a tried and tested Risk Management framework that enables Heads of PV to spot, record and mitigate drug safety risks before they take place, in a structured way.

The good news is, there is one out there and it’s already producing great results in Pharma Manufacturing. Early adopters are trialling it in their UK Drug Safety units, with a view to rolling it out across the globe.

The new approach merges proven methodologies such as Failure Mode Effect Analysis (FMEA) with best practice risk management in five easy steps. The first is identifying the risk – tracking information gleaned from sources such as questionnaires, audit reports, meetings and conference calls. Step 2 is Analysis – what system/process/component is affected by the risk. Impact – how big



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is the risk if it happened? Could it harm the patient, the business, or both? Each risk is assessed and scored as to its scale of impact. Calculate the likelihood of it happening by the scale of impact and you have your priorities, and a clear indication of where to focus your resources.

The next step is a plan of mitigation actions to stop the high priority risks turning into anything more serious. This is followed by 'Control and Report', which enables you to track and monitor your actions. Monitor the risks continuously as work takes place – is there a chance the risk could return? Take it through a risk cycle until you are sure it is completely mitigated. The result? A safer environment and a proven structure for managing risk that proves to the regulators and shareholders that you are practising towards proactive pharmacovigilance.

Conclusion

PV heads face many new issues and effective implementation of the resulting changes will rely on their ability to transform their organisation making best use of processes, technology and skills.

To manage this transformation PV Heads will need to leverage their metrics and communications capabilities. This increase in change readiness will be vital to their future success in the new proactive PV environment.



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