

The first rule of pharma is to do no harm

Periodic safety update reports can be seen as a time consuming exercise or as a positive step towards proactive pharmacovigilance. Chris Holmes explains how to stay one step ahead.



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No-one likes reporting bad news, especially when it can lead to the withdrawal of a product. Equally everyone knows it is better, particularly in pharmaceuticals to play safe. This ambivalence is squared in most companies by simply doing what is required by law.

But current regulations are not easy to comply with and some firms are finding it pays to be more proactive in their pharmacovigilance efforts. Bayer, for example, has taken the decision to compile periodic safety update reports (PSURs) on 60 or so of its strategic drugs every six months, rather than adhere to the timetable of the regulatory authorities.

This decision has taken significant resources to implement, but it provides a continuous process of safety evaluation and a 60% reduction in the cost of producing each PSUR. The extra costs come from implementing 'smarter' drug safety processes to simplify activities, improve productivity, and provide better quality information to both the affiliate companies and the regulators.

Pharmaceutical firms receive information on hundreds of adverse drug reactions (ADRs) every month. Every case must be evaluated, prioritised, processed and submitted to the authorities in such a way that gives them a clear company view of a product's safety profile. This is made harder as individual physicians tend to write in their own detailed scientific style.

This data must be incorporated into the PSUR, along with input from various other departments such as sales to help define the relative frequency of safety signals. Similarly, when actions proposed in the PSUR result in a change to the core data sheet and, possibly, in product labelling, the repercussions are felt across numerous departments.

Compiling data, and dealing with the effects of that data, across departments is made more complicated because the pattern of deadlines for reports is not smooth across the year. The regulations insist that reports must be submitted every six months for the first two years after a product is registered, annually for the next two years, at the first renewal of registration, and five yearly thereafter.



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This schedule for PSURs restarts whenever and wherever that product is registered (except the US) and with each product line extension. If the deadlines for reports are not harmonised around the world, workloads can easily become unbalanced and inefficient.

Indeed, the reason Bayer started transforming its pharmacovigilance processes was largely to smooth out the workload, particularly around the data lock points (DLPs) for each submission. Specifically Bayer wanted to comply with regulators' demands for information to be up-to-date but with minimum disruption to its normal processes for detecting signals from adverse events. The company realised it needed a process that could continuously review safety information and report more frequently to the regulators. Having changed the company processes, it is now only necessary to write summaries of safety statements at the DLP.

This kind of proactive approach is becoming increasingly common as companies such as Pfizer, American Home Products and Eli Lilly move in the same direction. Another reason for this trend is that US policy on pharmacovigilance is expected to align itself more closely with that of the rest of the world in the near future. The FDA is said to recognise the superiority of the PSUR over the 'periodic' reports that are used in the US and is preparing regulations to migrate towards the International Conference on Harmonisation E2C format. The agency has stated that periodics are 'often little more than data dumps' and that 'PSURs are more comprehensive'.

A main goal towards becoming more proactive should be to increase PSUR frequency for all key products to six-monthly reports irrespective of the due date; and to make these available to country affiliates to download off the intranet as and when required

This allows a company to have a consistent and up-to-date view on safety, providing the key tool to support proactive signal detection. However, trying to achieve this within current processes could mean a significant increase in resources. The alternative is to tackle the complexity of current ways of working by:

- Re-establishing responsibilities for timeliness and data quality in drug safety departments and establishing visible measures of performance.
- Reducing the need to chase information by giving 'supplying departments' a schedule of what is needed throughout the year and, again, measuring this visibly.
- Creating a simple template for the PSUR that can be used each time and eliminates what is not needed by authorities. Lack of consistency in format and content adds significant time in compilation.
- Redefining the PSUR content using keywords, phrases and predetermined outcome statements which eradicate the need for personalisation and unnecessary narratives.



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- Balancing the workload by spreading PSUR activity across the calendar to minimise unnecessary work and only adding new information when necessary rather than rewriting.
- Providing a means to review sources of safety information continuously rather than collectively when the reporting period is complete to avoid peaks in workload.

Cross-training staff between therapeutic teams and using visible metrics helps to improve performance in quality, consistency and timeliness. Likewise, the assembly of a comprehensive PSUR schedule which includes both static data (such as chemical/generic names, international birth dates) and dynamic data (harmonised submission due dates, individual department due dates) is critical for meaningful capacity analysis, resource planning and workflow scheduling.

But all this is just a step on the way to becoming truly proactive in pharmacovigilance. As Dr Ernst Weidmann, Head of Global Drug Safety at Bayer says, this is ultimately for everyone's benefit. 'The industry has to find the resources and more efficient ways of producing PSURs if it is to enable effective and proactive signal analysis,' he says. 'But we must make them digestible for the agencies who have to assess thousands of reports for accuracy of safety data. Furthermore we need to go back to the ICH guidelines, get away from overly detailed review of items which are not important and concentrate on looking for new, important safety signals on a proactive basis.'

This article was published in Scrip magazine, January 2001. The author can be contacted at chris.holmes@wcigroup.com



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