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SIGNAL DETECTION HAS BEEN A VITAL part of the pharmacovigilance (PV) process for years. However, data reporting complexity and growing expectations from regulators to be more proactive in predicting adverse events is changing how signals are captured and addressed.

A signal is a piece of information that suggests (but does not prove) a potential causal association between an intervention and an event, indicating the possibility of unintended outcomes. In extreme examples, a signal might uncover a rare but dangerous side effect in a marketed drug that did not emerge in clinical trials.

Originally, signal detection was a reactive process. If an adverse event, such as a heart attack, was reported by a patient or their physician, related to a specific treatment, the report would be studied and further actions might have been taken if the signal proved reliable, relevant and meaningful to the context of the treatment.

The flaw in this approach is that patients and physicians do not always report adverse events in a complete and structured manner, as in a clinical trial setting; particularly if they are mild, or seemingly irrelevant to the treatments they are using. In addition to spontaneous reporting, adverse events are captured in even less formal formats, such as social media posts, chatbot discussions, journal articles, handwritten documents, customer call-in centers and other unstructured narrative settings.

That means that valuable information about potential signals is out there, and regulators increasingly expect PV teams to find it and follow up as part of their safety monitoring process. These expectations, coupled with the increasing quantity and complexity of PV-relevant data sources, are transforming the signal detection culture into a more proactive process that can no longer be managed by human analysis alone.

Treatment-relevant signals are often buried in vast data bases. Imagine trying to search all of Twitter for references to a specific treatment side effect or reading every journal article that mentions a certain condition. These data sets are huge and often unstructured, requiring that signals be detected within a broader, unstructured narrative rather than lifted from carefully completed fields. This results in a data set of reports in which the complete medical story of the patient is not known.

To adapt to this variable source and quality of data, many PV teams are looking toward artificial intelligence (AI), natural language processing (NLP), machine learning (ML) and analytics tools that can be taught to search for signals based on key words, phrases and trends rather than the more traditional proportionality analysis used for product: event pairings in a structured data set.

For example, natural language processing can be applied to the full text content of a potential signal. Using algorithms to look for potential AEs based on the sentence structure and context of the report, technologies using NLP and machine learning can, over time, be taught to “read” any source information. With the right training, these algorithms can conduct rapid and sophisticated analyses, proactively identifying signals that may hint at a hidden problem.

Not (Yet) Mandatory

Proactive signal detection methods are not yet officially required by regulators, but they are considered part of good pharmacovigilance practices (GVP) and referenced extensively in the European Medicine Agency's GVP Module 9 guidance document.

More importantly, when pharma companies make proactive signal detection part of their PV monitoring, they reduce their risks and increase the chances of positive outcomes – even when adverse events are discovered.

Proactive signal monitoring, using AI and ML tools, allows them to uncover signals faster by analyzing much broader and more diverse data sets. Not only does this demonstrate their commitment to safety, it can provide them with the time to adapt a label claim or treatment paradigm to potentially keep a drug on the market.

Consider Tysabri, Biogen Inc.'s highly effective multiple sclerosis drug. In 2005, Biogen and Elan voluntarily withdrew the product from the market after discovering that 1 in 1,000 patients were at risk of progressive multifocal leukoencephalopathy (PML), a rare but dangerous brain infection. A year later, the US FDA allowed the product to return to market with a "black-box" warning after Biogen developed a screening process to identify patients at higher risk of contracting PML.

Thanks to early signal detection and a proactive response strategy, Tysabri was able to return to the market under a Risk Management Plan from FDA including mandatory genetic screening for the risk of PML, and MS patients continue to benefit from the product.

By adding next generation AI and ML to tools such as IQVIA's RxProfilerpharma companies can optimize their signal surveillance process in a simplified manner to monitor risks across multiple data sources. It requires investment in new technology and in culture change efforts, but the results will drive efficiency, reduce waste and create a safer environment for patients.

***About the author**: Miranda Greenhalgh has more than 14 years' experience and a background in management, regulatory affairs and data analysis using SQL, BO, Clintrace, ARISg, Argus, Oracle AERS, SAS and a number of other software packages for signal detection and aggregate reporting. Prior to joining Foresight and IQVIA, she was a product manager and SME in the industry and worked in multiple roles with safety organizations including Sunovion, Genzyme, and small CROs. Miranda is also an adjunct professor for Regulatory Affairs and Safety at Northeastern. how signals are captured and addressed.*

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