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Adverse Event Reporting: When TMI is Risky

By Bill Myers

As sponsors and sites have expanded their global reach, they've run into myriad local and regional regulations requiring them to report adverse events in their clinical trials. Hoping to simplify, many sponsors or sites have tried to create a one-size-fits-all form that sends out nearly automated alerts for nearly every single glitch.

"A lot of pharma companies take the approach that they've got to be compliant with everyone, so they say, 'We'll just send out everything,'" says Steven Beales, WCG's senior vice president for safety. That might sound OK. [But] you're wasting site hours and you're not improving safety because you're diluting the message."

A decade ago, for instance, Roche discovered that it was distributing more adverse event warnings from trials than any other drug developer, with nearly a million notices going out to patients, regulators and others at a cost of more than $75 million in one year. As the company expanded through mergers and acquisitions, it was looking at having to dispatch in excess of 25 million alerts every year, Beales says.

The root of the problem was the scattershot regulatory regimes across the globe — Beales and his colleagues analyzed worldwide clinical trial regulation and found at least 40 different variances. "Patient safety is obviously the most important thing we do and sometimes that responsibility is put onto the regulatory agency, sometimes onto the site, sometimes on the ethics committees, sometimes on the CROs, sponsors," he says.

An "adverse event" can be nearly everything from a slight itch to death and most rules require reporting it whether or not there's conclusive proof that the treatment is the culprit. According to the FDA, there were more than 1.8 million drug-related adverse events last year — about half of them considered serious. That number includes drugs that are already on the market but it suggests an enormous problem for drug sponsors and sites.

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Overwhelmed by the regulatory burdens, many sponsors or sites simply err on the side of caution and send out alerts for every incident. But there's no guarantee that the alerts are making a difference for either the company or the patients. Mass emails, for instance, might say all the right things about an adverse event, but companies have no way of ensuring that patients have actually read them.

"They're really sending them out blind. That opens up you up to inspection or compliance. Because the inspectors will say, 'OK, you say you've notified so-and-so. How do you know the email arrived? How do you know they've read it?'" Beales says.

Given the sheer volume of alerts, it's hard to know if patients are reading them all if any, Beales says, noting they may be so common that patients simply disregard or dismiss them as insignificant.

Despite efforts to bring international regulations into alignment, it's unlikely that reporting requirements will get substantially easier. In January, for instance, *The Oncologist* carried an op-ed urging the FDA to include data about the duration of an adverse event in its reporting requirements.

Whether or not that idea catches hold with regulators, Beales estimates that site staffs are already spending an average of 10 hours a week just reporting adverse events.

The good news, Beales says, is that technology has now made it possible for companies to hone their focus. Advanced algorithms, once in place, can help determine whether an event needs to be reported, and if so, by and to whom: Should an alert go to patients? Regulators? Sites?

Beefing up a company's alert system isn't easy and it's not always cheap. It requires a soup-to-nuts approach, beginning with an audit. That can sometimes be a logistical nightmare, especially at the outset. The first year that he worked with Roche, Beales says, he and his colleagues discovered the company was actually under-reporting events by 2 million cases.

A warning sign might be that a company doesn't actually know what it costs to send out alerts, Beales says.

"If they go through their contracts, they're going to go, 'We can't work out what we're spending on this. We don't have a clear idea of whether we're compliant,'" Beales says.

So, is it worth it to discard the one-size-fits all approach and go through the arduous route to a tailored alert system? Last year, Roche saved a hefty $65 million by personalizing its alert system, Beales says.