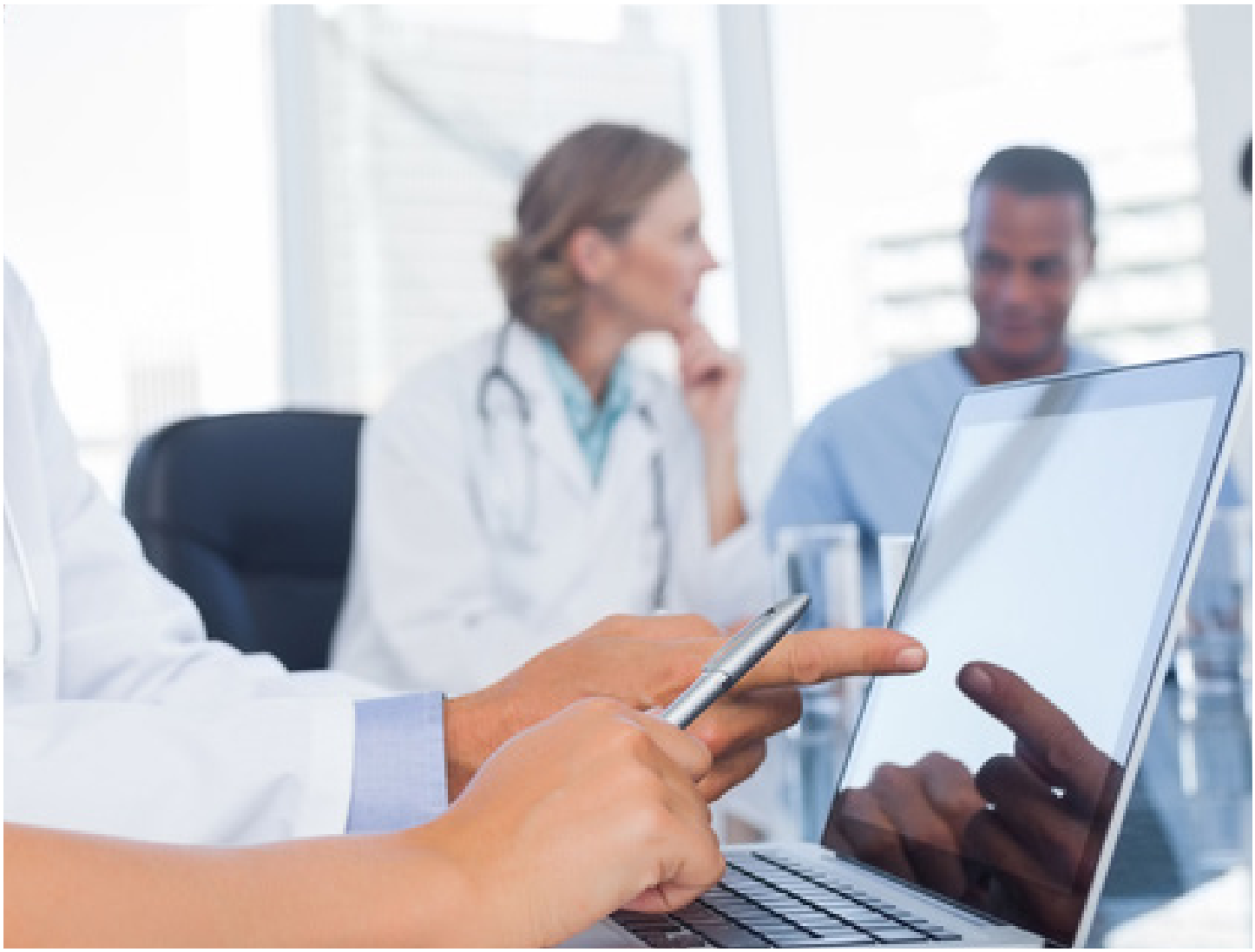

Something Has to Give: The Current Unsustainable Approach to Safety Reporting Puts Trials and Patients at Risk

Steven Beales, SVP, Safety Solutions

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Safety reporting may be the most inefficient aspect of clinical trials today. It's also among the most expensive, costing sponsors more than $700 million per year. Most are not receiving the best value for their investment, and some don't even know how much they are spending. Automation has helped resolve some of the challenges, but it has created just as many. The system needs a complete overhaul. It can be done, but it requires the willing to invest in change.

The current approach to safety reporting places a heavy, sometimes unmanageable, burden on sites: Sponsors bombard sites with safety notifications, much of them unnecessary. The sites risk being overwhelmed to the point they miss the critical patient-safety information. Then there's the issue of global harmonization. Sponsors, too, become overwhelmed. For large trials, they must keep up with hundreds of different—and constantly evolving—country-specific rules.

The entire process is not only costly: It is ripe for error, and the consequences can be severe. Patient health is the most important issue, but far from the only one. One mistake can lead to regulatory repercussions, delays—even having a trial go into rescue or be shut down. Even if the current trial remains unaffected, sites are disinclined to work again with sponsors who bombard them with superfluous, burdensome paperwork.[1]

Exponential effect

A single incident can generate a tremendous amount of paper. For a large pharmaceutical company or CRO, the scale is enormous—with tens of thousands of notifications being distributed every day to dozens of countries. Each country may have its own particular rules and regulations.

Almost as important as distribution is auditability. Sponsors must be able to drill down and show that the notification was sent out, that it was sent to the correct person, that they received it and, in some cases, even that they acknowledged and understood it.

Joe O'Rourke, vice president, business development at WCG, points to a top 2 pharma as an example. "At the largest pharma or CRO scale, they have to send out, or attempt to, 25-50 million letters or notifications each year. To put that into context, that's over 75,000 a day. It's relentless."

To solve that challenge, a top 2 pharma turned to WCG. WCG's SafetyPortal streamlines safety report distribution, confirms that only those who need to see the document receive it, and ensures compliance with the regulatory bodies of 110 countries. By automating its process with WCG's *Clinical Trials SafetyPortal (CTSP)* solution, the top 2 pharma not only remains compliant, it saves about $150,000 per study.

Most sponsors have yet to revamp their safety reporting systems, although many have moved to more automated approaches.

Automation and chaos

In the past, sponsors would typically fax letters or use an overnight service. It was inefficient and often expensive, with no assurance the notifications reached the appropriate parties. Some sponsors still use these approaches.

Electronic Solution	Overnight	Email	Fax
Automated acknowledgement tracking and reporting capabilities	Poor tracking of receipt by investigator	Cannot confirm receipt	Hard to confirm intended recipient received the fax
Dependable distribution algorithms	Package may make it to PIs facility, but not the individual themselves	Mistakes are made when spelling recipients email address or choosing from pick list	Potential for incorrect fax number to be entered or safety doc gets accidently picked up by unintended recipient
Real-time distribution worldwide	Delay in investigator receipt due to shipping and slow internal courier services at the medical facility	Emails get caught in spam filters delaying receipt	Delayed fax distribution in large facilities
Secure sign-on	Once delivered, safety document can be viewed by anyone if not secured	No authentication required to access safety document	Safety document can be access by anyone who has access to fax machine
Audit Trail reporting	No audit trail	No audit trail	No audit trail
Instantaneous Gap Pack at time of site activation	Delayed receipt of gap pack due to manual labor of packing and shipping	Manually compiling safety documents could lead to missed documents	Room for error when faxing large numbers of documents

Many sponsors, however, are moving toward automated approaches—at a minimum, email. This allows sponsors to easily send out more safety letters more quickly, but that creates a new set of problems, says Steven Beales, senior vice president, IT, and market owner, safety solutions at WCG. The attitude, he says, is this: "Well, if I send too many notifications, that's not going to be a problem, is it?"

But it is a problem, he warns. "It drowns the site in unnecessary emails, burying important safety information in a pile of noisy, unnecessary documents."

The logic behind this scattershot approach does make sense, to a point. Sponsors' safety reporting systems don't accommodate the regulatory variations among countries. To avoid non-compliance, they move in the opposite direction and overdistribute.

From discord to harmony

"If you talk to pharma execs, they will tell you that their biggest headache is the lack of global harmonization," Beales says. "Each country has a set of regulations governing this and you would think they would all be harmonized."

You'd be wrong.

There're at least 40 different approaches in terms of how countries handle SUSAR distribution. The solution isn't to distribute as many notices as possible, but to carefully target distribution, giving each site what it needs to be compliant without overwhelming them.

WCG's SafetyPortal harmonizes regulations for 110 countries, so sponsors can distribute SUSARs based to what the laws specify. That avoids sending a SUSAR when it's not necessary. It eliminates roughly 40 to 50 percent of all SUSAR notifications, because they are unnecessary, Beales explains. "We have all the regulatory intelligence, and our system uses that to make the intelligent decisions about what needs to be distributed."

Because the system is continually updated, sponsors remain in compliance because each site receives the notifications it needs. "For some of our largest customers, that may be the biggest benefit," Beales says.

Similarly, IRBs and ethics committees have varying requirements. Consider blinding. In 22 countries, the ethics committee requires unblinded data. That's usually a separate, cumbersome, manual process

carried out by another team at the pharma company. WCG can automatically send it blinded to those for whom it needs to be blinded, and unblinded to anyone who needs to see it unblinded.

The power of inertia

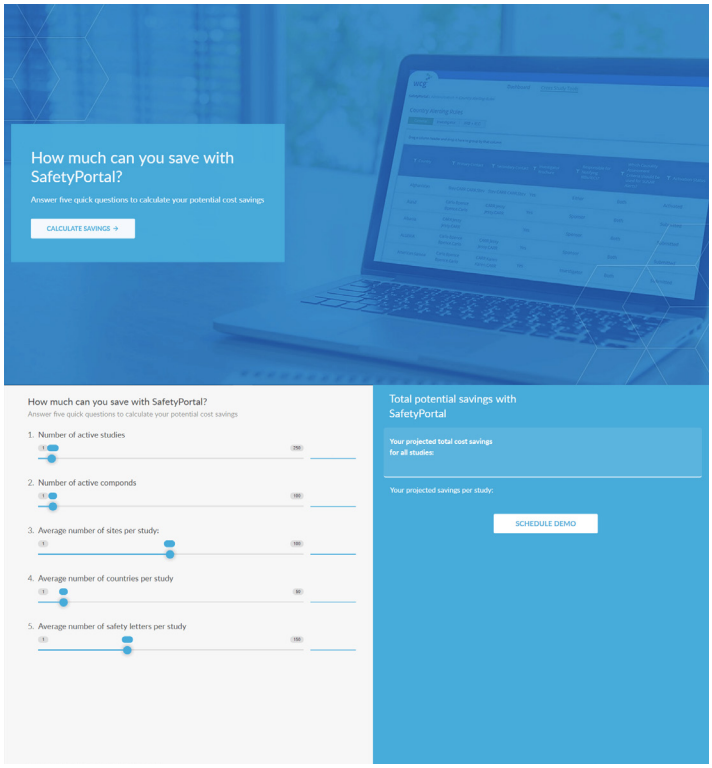
"If you talk to pharma execs, they will tell you that their biggest headache is the lack of global harmonization," Beales says. "Each country has a set of regulations governing this and you would think they would all be harmonized."

No one would dispute that the current system is deeply flawed, and various vendors have tried to fix it. The problem is the system can't be "fixed." It demands a complete overhaul.

O'Rourke uses the metaphor of mass transit to explain. "Here in the Philadelphia area, we have SEPTA and Amtrak train systems. The trains arrive roughly on time, but they're very inefficient, outdated and overly manual to operate. There may even be safety issues. But here's the problem: Uprooting those trains and putting in a new, more efficient high-speed train system would be a big process."

The way pharma companies handle SUSAR distribution today is comparable. Changing out a few cars, hiring new conductors—or even replacing all the engines—won't solve the problem.

The system must be gutted and rebuilt. That requires an upfront investment, but it yields a tremendous return. "We usually come up with something like "spend a million, save ten million,'" says Beales.



Why walk away from that ROI? "Because it's all future dollars, and there's work to realize those savings. And many sponsors don't realize how much they will save, because they don't know how much they are spending," he explains.

And that gets to another challenge: Safety reporting is a hidden cost, and until they realize how much they are spending, they aren't inclined to invest in a solution.

Transparency and tracking

Because so many sponsors are negotiating budgets study by study, they aren't quite sure how much safety distribution should—or does—cost. Beales has seen sponsors spend anywhere from $100,000 to $2 million per year—on one study. One reason the costs remain hidden is that a sponsor will often hire a third party to take it off their hands.

Even worse, sponsors rarely have a way of knowing that all the appropriate documents were sent to all the appropriate parties. So when an inspection or investigation occurs, they discover that the notifications were never received by the appropriate parties. Or perhaps more accurately, they discover they cannot verify receipt, which is essentially the same thing for audit purposes. One client was underreporting events by 2 million cases, despite its scattershot approach to distribution.

To adequately monitor compliance, sponsors need to be able to track a particular SUSAR to a particular Investigator. "We can do that at the protocol, compound or sponsor level at the click of a button," Beales says. "Because we've embedded trackers in our emails, 98 percent of the time we can tell when an email arrives in someone's mailbox without needing them to click a link to provide an acknowledgement. Our system tracks every touch and reduces the need for a site to take steps to demonstrate they received a notification." Sponsors have complete transparency; they can click a button and see how many Investigators and sites are compliant, when they last logged on and who hasn't acknowledged what. "If you've got 50 million of these distributions to monitor annually, you need a bulletproof monitoring and reporting system to handle that scale," he says.

Lift the burden: simplicity and streamlining

For the investigator, all of this should happen behind the scenes, so the user experience is simple. SafetyPortal has a clean interface that allows Investigators to focus their time on research, not on trying to access the dashboard. As an associate director of regulatory affairs for a large university medical center recently commented to Roche, "This seriously is a phenomenal system compared to other sponsor pharmacovigilance processes."

The simplicity of the site experience is only part of it. Let's say there are eight studies in one therapeutic

area. SUSAR distributions occur at the compound level. That means the same SUSAR goes to eight separate studies—each study using that compound. In a traditional system an Investigator working on three of those eight studies received the same document three times and had to acknowledge it each time.
"Our system solves that problem, says Beales. "You get the document once, you acknowledge it once and you get credit for all the studies you're working on."

That level of automation also reduces human error. Data entry error is very common in our industry. In our system, data entry is avoided; we offer an entirely automated process. It's all coming from the sophisticated integration WCG has with clinical trial management systems, safety databases, trial master files, shared investigator platforms, etc.

Reducing the site burden improves patient care. Sites can redirect the time spent managing safety documentation to working directly with patients. They can also better ensure patient safety. When sites receive only the relevant notices, they can actually address the safety issues with patients.

No more patches

FThe current approach to safety reporting is costly and inefficient, burdening sites, frustrating Investigators and putting trials in jeopardy. Worst of all, it puts patient safety at risk. The only solution? Build a better system from the ground up.

That's what WCG offers. WCG's SafetyPortal helps clients improve safety, efficiency and compliance while saving millions. As of May 2019, WCG will have more than 215 sponsor and CRO clients for its SafetyPortal solution. If your organization is ready to meet the challenge of global safety reporting, contact us at **jorourke@wcgclinical.com** or visit **www.wcgclinical.com/services/safety-portal/.**

About the Author

Steven Beales, SVP, Safety Solutions

An expert in the field of safety reporting technology, Mr. Beales has 25 years of experience in IT, and has spent over 16 years in the pharmaceutical industry. He joined WCG ePharmaSolutions in 2009 and led implementation of the company's Clinical Trial Portal at Genentech across 100+ countries. In 2015, he led implementation of the Clinical Trial Safety Portal at a top 5 pharma organization, which included a data-driven rules engine configured with safety regulations from those countries, which saved this organization hundreds of millions of dollars. Over 50 million safety alerts have been distributed by these two portals via the cloud.

Prior to joining WCG ePharmaSolutions, Mr. Beales was the Chief Software Architect at mdlogix, where he led the implementation of the CTMS systems for Johns Hopkins University, Washington University at St. Louis, the University of Pittsburgh, and the Interactive Autism Network for Autism Speaks.

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[1] "Managing the Unmanageable: Meeting the Challenge of Appropriate Safety Report Distribution" WCG 2017

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