Optimizing SUSAR distribution in a connected–but unharmonized–world

In conversation with... Steven Beales & Joe O'Rourke

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Safety reporting costs biopharmaceutical companies over $4 billion per year[1], but because it's a hidden expense, many sponsors are unaware of just how much they are spending. The current approach is resource-intensive and prone to error. Sites receive such an overwhelming amount of information from sponsors that they risk overlooking critical patient safety information.

Then there's the issue of global harmonization. Sponsors often need to follow hundreds of different country-specific rules. It is difficult to conduct this global process correctly and the consequences of making mistakes are severe, including potential risks to patient health, regulatory repercussions, delays–even having a trial shut down.

WCG's Clinical Trials SafetyPortal (CTSP) helps clients solve these problems while improving compliance and saving money. As of May 2019, WCG will have more than 215 sponsor and CRO clients for its CTSP solution.

To help better understand what's involved, we turned to Steven Beales, senior vice president, IT, and market owner, safety solutions at WCG and Joe O'Rourke, vice president, business development.

Steven Beales

Joe O'Rourke

In this interview, Steven Beales, senior vice president, IT, and market owner, safety solutions and Joe O'Rourke, vice president, business development talk through some of the difficulties Sponsors face when it comes to safety letter distribution, and how to overcome them.

The interview has been edited for clarity and length.

Q A

To bring readers outside the industry up to speed, can you give some background?

Joe O'Rourke: Let's say a patient in a trial gets an IV infusion or oral dose of the therapy. They suddenly pass out and wind up in the ICU.

That triggers a regulatory process. You must notify everyone else who's working on that investigational medicinal product worldwide. That process is commonly referred to as initiating a SUSAR. You're informing everyone of a **S**uspected **U**nexpected **S**erious **A**dverse **R**eaction. A SUSAR letter must go out generally within 15 days after the sponsor is notified of the event (seven days in case of death or life-threatening issue)–or at least that's how most sponsors treat it. The reality is far different and varies by country.

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Most sponsors believe the notification has to go to every Investigator working on that therapy as well as the IRB or ethics committee. When you're a large pharmaceutical company or CRO, the scale is enormous–with tens of thousands of notifications being distributed every day.

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Do you have a specific example?

Joe O'Rourke: Sure. Let's use Roche as an example.

Roche is our flagship customer. At Roche's scale, they have to send out, or attempt to, about 50 million distributions or notifications per year. To put that into context, that's over 125,000 a day. It's constant. It's relentless. (For more on Roche, see accompanying sidebar.)

And it needs to be performed in the most precise way, in an auditable fashion, you need to be able to drill down and show from inspection or audit at any time that the notification was sent, that it was sent to the correct person, that they received it and, in some cases, even that they acknowledged and understood it.

Steven Beales: In the past, this process was all done with FedEx, fax, etc. So it was horrendously expensive. It used to cost something like $75 dollars to send out one of these notifications.

By automating the process, Roche saves about $200,000/study/year. Moreover, large sites supporting many studies save an average of 10 hours per week. Compliance was above 99 percent. So, those are the outcomes people get by adopting the system.

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So some sites are still using fax or courier?

Joe O'Rourke: Steven and I were just on a call with one of the largest pharmaceutical companies in the world. Many of their sites around the globe use fax; there's not a good alternative for them.

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And your system would still work for those sites?

Joe O'Rourke: Yes. We can get them for pretty much 100 percent of the sites and most of the largest ethics committees. We've found this level of digitization and automation of distribution to be unparalleled.

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Q A How are you converting ethics committees to automated receipt of safety notifications?

Steven Beales: WCG is the largest IRB in the U.S. Our large pharma clients also recognize the problem and are addressing the issues with their own ethics committees. From there, it will be a mix of getting as many as possible online, but also solving that "last mile" problem. So even if the site or IRB insists on paper, it still goes through our system. Then someone from the client hands it over at the end of the line. But until that proverbial last mile, it's part of our system.

There's another important issue relative to IRBs/ethics committees: blinding information. 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. We're able to automatically send it blinded to those for whom it needs to be blinded, and unblinded to anyone who needs to see it unblinded.

Q A This seems like a good point to bring up global harmonization.

Steven Beales: If you talk to pharma execs–I was just talking to one yesterday and he said, "My biggest headache is the lack of global harmonization." So, yes, it's a big problem.

But our system has all the local laws embedded into it. 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. Our system has all that intelligence and then it distributes SUSAR only according to what the laws specify. We harmonize distribution regulations for 110 countries.

That avoids sending a SUSAR when it's not necessary. Somewhere between 40 and 50 percent of all SUSAR notifications are eliminated, because they *are* unnecessary.

Here are two simple examples. In Australia they say, "Please, don't send us those notifications straight after every event happens. We would just like to be updated every six months with a line listing." In the U.S. we say that if the doctor thinks the drug caused the problem, but the sponsor company disagrees, don't send out the notification. So, our tool has this level of sophistication built into to it and that's what makes it the market leader.

Q A How does this compare to other systems?

Steven Beales: Most of the other vendors in the space say, "Give me the list of emails. Give me what you send. I'll send it to everybody." And because people think, "Well, if I send too many notifications, that's not going to be

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a problem, is it? Doing more than necessary, that's not a problem." But actually, it is: It drowns the site in unnecessary emails and causes them to miss the really important pieces of information. In fact, sending too much is almost a bigger problem than sending too little. Now the sponsor is spending far too much and burying important safety information in a pile of noisy, unnecessary documents.

They aren't increasing efficiency.

What we're offering is far more than that. We have all the regulatory intelligence, and our system uses that to make the intelligent decisions about what needs to be distributed. That reduces what goes to a site and takes a big burden off the pharma company in terms of needing to keep up with all of this regulatory intelligence themselves. For some of our largest customers, that may be the biggest benefit.

Q A Given the challenges sites, sponsors and CROs face, what's the rationale for sticking with a broken status quo?

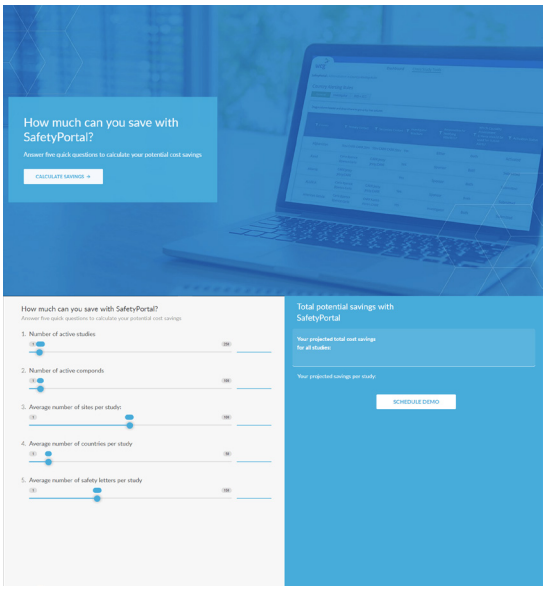
Joe O'Rourke: Here's the metaphor I use: In the Philadelphia area, we have SEPTA and Amtrak train systems. And the trains arrive roughly on time, but they're very inefficient. They're outdated and overly manual to operate. There may even be safety issues. But here's the problem: Uprooting those trains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

Pharma companies handle distribution today. They have a process in place to get the trains from point A to point B, even if it's overly manual, inefficient, etc. And so, oftentimes, it takes a while to either identify that there is an issue or there's an opportunity for growth and they want to make that change. And so, in most cases, inertia is our biggest enemy.

Q A That's costlier than the status quo, right?

Steven Beales: Not in the long run. We have a simple calculator to make the business case. We usually come up with something like "spend a million, save ten million."

Why would people walk away from that? 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.



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We also need to make clear we aren't just offering another piece of technology. A lot of companies don't recognize that we offer a solution and the expertise to guide them through it. It's not like installing Microsoft Word out of the box.

But yes, it is an investment, not just financially, but–as with the example of the train system–in terms of scope. It requires a workflow overhaul.

Q **Evidently, you need to do a lot of client education.**

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Joe O'Rourke: So much of this is uncovering things for the sponsor. We begin with an audit. We go in and say, "This is what the landscape actually looks like for you." It's an eye-opening experience–if they don't already know it, which most don't. Steven and I worked with one sponsor for almost a year and after 10 months we had to go through their budgets with them and uncover what they were *actually* spending because they couldn't figure it out for themselves. It had become *that* hidden within their budgets.

One reason is they are negotiating budgets study by study and are not quite sure how much safety distribution should cost. We've seen anywhere from $100,000 to up to $2 million being paid on one study to do this process manually or through third-party distributors.

Q **They aren't tracking the costs?**

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Steven Beales: It's often a "Let's just hand that over to someone else and they'll take care of it," kind of thing. They're almost unaware of what needs to go on around the world. A sponsor may send it to one person in each country and say, "Take care of your country." Or sponsors simply pay a few thousand dollars per site for a third-party distributor; the cost becomes buried and is not closely monitored.

Q **But it doesn't always get taken care of, right?**

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Steven Beales: Right. When inspections happen, pharma companies get the unpleasant surprise. They thought this was all nicely taken care of and everyone was notified, but lo and behold, when the inspection happens, they find the parties never got any of these notifications. In contrast, our system is able to track every delivery at the protocol, compound or sponsor level at the click of a button.

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Q How does your system help sponsors monitor compliance?

A **Steven Beales**: Without our system, monitoring compliance and making sure these things are done are very difficult. You need to trace that particular SUSAR to a particular Investigator. If you don't have a system like ours, people are going through emails, checking DHL Worldwide receipts and finding that DHL gets rid of all their records every two years.

Transparency is one of the big advantages of the system and our system takes it further. Because we've embedded trackers in our emails, 98 percent of the time we can tell when an email arrives. Our system tracks every touch and reduces the necessity for a site to take steps to demonstrate they received a notification.

This means sponsors can have absolute confidence: If you're a sponsor you can click a button and see how many people are compliant--when they last logged on, who hasn't acknowledged what. You get the complete picture through the system. And this scales up to companies like we talked about. Like Roche, you've got 50 million of these distributions to monitor annually--you need a bulletproof monitoring and reporting system to handle that scale.

Q How do you avoid basic data-entry errors?

A **Steven Beales**: Data-entry error is very common in our industry. In our system, data entry is avoided; we offer an entirely automated process. It's coming in from other systems to seed it. We get something like 75,000+ data updates a day from our various pharma companies. That changes site study information. We don't manually enter any of the info into our system. It's all coming from the sophisticated integration that we have with clinical trial management systems, safety databases, trial master files, shared investigator platforms, etc.

Joe O'Rourke: Ours is just a much more automated, streamlined and efficient process.

Q In some ways, everything we've talked about has related to alleviating site burden, but can you address that specifically?

A **Steven Beales**: We have focused heavily on-site experience; it's now at the point where our training for Investigators is only a couple of minutes. We keep the user experience that simple.

Our systems take care of everything in the background without someone from the site physically logging in to a portal.

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."

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So, there's the simplicity of the site experience. And by reducing all that paper, we're saving sites all those hours and delivering only what they need to see. We also build it so it's an online archive. In the past, you'd have to print out every SUSAR you received, sign it, file it away. We act as an electronic archive that takes that burden off the site.

Again, it's about simplicity and streamlining.

Let's say there are eight studies on a particular drug. SUSAR distributions occurs at the compound level. That means the same SUSAR goes to eight separate studies--every study that's using that compound. In a traditional system if you're an Investigator working on three out of those eight studies, you get the same document three times and you have to acknowledge it each time.

Our system and a few others solve that problem, so you get the document once, you acknowledge it once and you get credit for all the studies you're working on. That's "cross reporting" and it's another way in which we alleviate the site burden.

Q A How do patients benefit, aside from the overall improved safety?

Steven Beales: The impact on the patient burden is significant, but indirect. First, there's the hours each site saves every week. That's time they can spend with their patients.

Perhaps more important, each time SUSARs come out, sites are supposed to use them to talk with their patients and check for the symptoms described. When sites receive only the relevant and important notices, they can actually address the safety issues with patients. When they are being flooded with information, there is a tendency for sites to throw it straight in the waste basket. Which they do.

If your organization is ready to meet the challenge of global safety reporting, SafetyPortal resolves nearly every obstacle to ensure efficient safety document distribution.

Contact us at **jorourke@wcgclinical.com**
or visit **www.wcgclinical.com/services/safety-portal/**

[1] Case Study: How Roche Optimized its Global Safety Reporting Process for Clinical Trials, WCG 2018 https://insights.wcgclinical.com/case-studies/how-roche-optimized-its-global-safety-reporting-process-for-clinical-trials

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Flagship client: Roche

Roche launched CTSP 1.0 in August 2011, and WCG completed the upgrade to version 2.0 in March 2017. The update addresses an array of issues, including harmonized country rules. By November 2017, Roche CTSP 2.0 was supporting approximately 300 compounds and 3,000 studies in 107 countries. As a system, it handles 46.9 safety report requests every minute.

Roche has significantly reduced over-distribution, reporting a 65 percent reduction in safety alerts transmitted compared with its previous process. This equates to a reduction of 1 million safety alerts per month since CTSP 2.0 implementation automated country-alerting rules.

Read the complete case study at insights.