THE FUTURE OF THE DELIVERY OF QUALITY

David Alvaro, Scientific Editor in Chief and Research Director, Nice Insight

Pharma's Almanac **Scientific Editor in Chief David Alvaro spoke with TriRx Pharmaceutical Services' co-founder, Director, Executive Vice President, and Chief Operations Officer Jim Scandura and Executive Vice President and Chief Quality and Regulatory Affairs Officer Don Britt about the importance of quality system and quality culture at CDMOs and how they are evolving.**

David Alvaro (DA): How would you personally define or characterize quality culture in pharma, and how have you seen it evolve over your tenure in the industry?

JIM SCANDURA (JS): You want to make sure that there's alignment between your operations and quality people. The quality folks are the ones that set the guidelines, but real quality happens across the organization, on the shop floor and in the labs. You have to have a culture within your operations group that results in everyone – from operators to their supervisors and managers, as well as site management – recognizing the extraordinary importance of quality. It only takes one moment of inattention to quality details to lead to a safety issue that could cause patients harm and put the company out of business.

DON BRITT (DB): It is definitely our philosophy – and it comes from owner, Chairman, and CEO Tim Tyson – that quality is everybody's responsibility within our organization. I truly believe we don't just say it; we practice it. The pharma regulatory environment is constantly changing. It's an everchanging regulatory environment that pharma is in. In our business, compliance and quality are the tickets to being in the game.

DA: What does it take for a CDMO to maintain a constant state of inspection readiness?

DB: We perform self-audits, so we're looking at the operation constantly and can fine tune and improve whatever we're looking at and auditing. In addition, we instill in our entire team the recognition that the medicines we manufacture are taken by TriRx employees and their children and grandchildren. And we all take pride in that.

In fact, audit preparation is one of the big differences between TriRx and Big Pharma sites. In our business, because we have so many audits – regulatory agencies, customers, and ourselves – it needs to be a core competency. If you can't do it on one or two days' notice, you're doing something wrong and wasting too much time.

At TriRx, that isn't an issue. A team would be ready immediately to coordinate with the customer, determining specific areas of interest and preparing documents. In addition, I don't know any other CDMOs where the CEO or the COO is so involved at the operational level, but that goes a long way to underscore to our operational teams how committed they are to the quality and compliance of everything that we do.

DA: What can you tell me about the organizational structure and the different stakeholders or departments involved in establishing and maintaining quality culture at TriRx?

JS: In the past, I have conducted operational audits commissioned by CEOs of about 35 different pharmaceutical plants. I looked at things like organization charts and interviewed all the leaders of specific groups. It was easy to tell right away when the attitude towards quality was not aligned. Typical comments were, "Well, they make us do this," with "this" meaning "quality."

If you get into a situation like that, where it's an us-versus-them kind of a routine that comes from the top, it doesn't work. That is a worst-case scenario; most of the time there

is simply a lack of clear alignment. The operations personnel are focused on getting product out the door, while the quality team is focused on compliance.

The real answer is that producing high-quality, compliant products is the responsibility of both operations and quality personnel. If that message doesn't come from the top of the organization, the different groups won't align themselves, and they won't do it. At TriRx, we focus on quality and regulatory compliance at all times from the top down, including me, the CEO, and the entire Executive Committee.

DA: What are the roles for new technologies in a modern quality system?

JS: When we acquire a site, we use a standard set of cloud-based tools, including SAP and Empower3 for data alignment. ZenQMS is our quality system for training, tracking, and document management. We don't make a lot of changes site to site but rather require other sites to operate within that mold. We make changes as we go along and back feed them to the existing sites, which establishes consistency across all activities.

Technology provides efficiencies and consistencies, as well as cost savings as we grow once those solutions are in place and are understood. These technologies help our expert communities, which help the sites set goals for their various activities (research, quality, etc.) to address important issues consistently.

Our goal is to operate our labs efficiently and effectively and to the highest quality compliance requirements. An FDA inspector once told me that he sees the QC lab as the last line of defense; if the QC lab has issues, there are likely much larger concerns. If the lab is operating perfectly, however, there is much less likelihood of quality issues existing in the plant.

DA: How does a CDMO go about differentiating itself on the basis of its quality culture and systems, and how do they project that outwardly?

JS: First, we should separate internal pharma manufacturing sites within Big Pharma companies from external service providers. Internal manufacturing groups have just one customer with one uniform set of processes and procedures and documentation requirements. External CDMOs with multiple customers must have adaptable quality systems that are both easily understood and easy to present to customers during audits. In addition, the way the audit is conducted and the individuals involved is really important to establishing the client's perception of your operations.

You want to have individuals representative of your entire group in the audit explaining to the customer how you approach quality. You need to have lab staff, operations teams, and supply people in the room, all understanding the customer's concerns and responding appropriately with a strong awareness of regulatory requirements and the customer's expectations. The perception is established at that quality audit regardless of the output, and that perception spreads throughout the client's company.

DB: One of the things TriRx does better than CDMOs I dealt with back when I was with Big Pharma is treating every single client as if that customer is the only client from a compliance/quality standpoint. Our team is also very transparent with our clients in that, if we have an issue, even though we resolve it quickly, we also immediately get them involved and let them know what we're doing with their product. That approach has really paid off for us.

DA: What do you identify as the absolutely essential criteria when selecting a successful CDMO partner, from the point of view of quality and compliance?

DB: A potential CDMO partner would need a pristine regulatory background history. I don't mean just the last inspection, but the last three to five years' worth of inspections, because warning letters are usually not issued unless there is a repeat or similar violation.

In addition, an FDA or other regulatory agency inspection is just a snapshot in time. They can't examine every system in a facility in the limited time of an inspection. If I see some significant issues, it makes me believe there must be others that the inspectors just didn't have time to find.

JS: There are other, maybe not quite red flags, but maybe yellow flags. For example, say a company had concerns four years ago, and they showed up in audits for a couple of years and then there were some management changes. If the only management change was the head of quality, you've got a problem, because the head of quality didn't cause those quality concerns. The operations people caused them, and the quality people caught them, which is what they're supposed to do. I'd be looking for changes in other areas, like site leadership, the head of the site, production people, everything that had to do with how the product is actually produced.

As you might imagine, we've had a significant history of acquiring new facilities. Our leadership team can – within the first five minutes – tell you whether we're interested in a factory.

When I was at Big Pharma and would meet with and evaluate partners, I would ask questions that have multiple answers. I'd invent scenarios that involve quality issues, and often they wouldn't have a quality person in the room, and no one could answer the question.

To me, that means they're not integrated. The people that are actually doing the work or moving the product into the plant don't really have an appreciation of what they have to deliver other than the technical details; so that's difficult. It seems to me it's obvious how to do it; but it just doesn't seem obvious to a lot of other organizations.

DA: Given that that it's much easier to retain a customer than to find a new one, it seems short-sighted to not be better prepared. Shouldn't that be obvious?

JS: It is obvious, and here's why. You have long-term agreements with these customers, and if you're putting out a good product on-time, in full, at a reasonable price, and compliant, that customer has no reason to change. The only reason they change is that they're not satisfied with what the CDMO is doing, because it's expensive to change. It's a regulated industry – heavily regulated –

Big Pharma companies are contracting more and more operations, and I believe that trend is going to continue. If you're going to be a big player in our business, you must have quality systems in place and keep your compliance record up, or you won't be in business.

and expensive. You get a new customer, you try to keep them for life.

It's amazing to see how many of our clients come to us because they're dissatisfied with their current supplier. If somebody told us that they were very, very upset and were looking at moving this product – we would move heaven and earth to get that customer satisfied.

DA: What are some red flags that might suggest that a CDMO's quality culture/ quality systems might be lacking?

DB: A big red flag is a lack of transparency with their clients. You can certainly get a feel for how a manufacturing operation is run from a compliance/quality standpoint, not just from the sheer number of 483s, which are the observations that the FDA leaves, but how significant those observations are. Obviously, we share our regulatory inspections with our clients. Our quality history from a regulatory standpoint is exceptional.

JS: Every audit contains a tour. What I always found helpful when I was on the audit side is: Who do you meet on the tour? How do they act? What do they show you? Are there areas they don't want you to explore? It can be obvious. If you're an experienced auditor, it's obvious to you when the organization under audit wants you not to find something or enter an area where you're not supposed to be.

At TriRx, our tours are quite open. We let people see whatever they'd like to see. Typically, the auditor will come in and tell us the areas where they want to focus or specific responsibilities they want to focus on, and we take them right away to see them. It's who you meet, how you operate during the audit. The transparency Don talked about is really important. It's not a game. Customers rely on us to provide life-saving medicines for patients in the market. If we don't provide them in a way that ensures quality, then they fail and we fail; it's a bad outcome.

DA: Aside from more formal audits, what are the best ways for a customer to follow along and assess quality control and assurance during the execution of a program?

DB: We have routine meetings, typically weekly, in which the quality teams from both companies participate. We work very closely with the quality organizations to make sure that what we're doing aligns with their expectations.

JS: In addition, as we generate contracts and supply agreements, we also generate a quality agreement between the organizations that specifies in all cases what is acceptable to the customer and the periodicity. For instance, if any material is out of specification or out of trend, we notify the customer as soon as possible.

I've seen other organizations where they constantly push the envelope of the quality agreement. You can't do that, and we don't do that. You've got to have a good relationship with the client's organization at every level, or things are going to go wrong with the transfer.

DA: What does the future of quality look like to you?

DB: The future looks very promising. Big Pharma companies are contracting more and more operations, and I believe that trend is going to continue. If you're going to be a big player in our business, you must have quality systems in place and keep your compliance record up, or you won't be in business. Tim Tyson and Jim Scandura have that same philosophy, which is a big reason I'm with this company. I know how they operate and how they don't just speak the word "compliance" and "quality;" they live it every day.

JS: I hope the future brings defined ways to be compliant in a consistent way across the globe. I don't see it happening right now, but I think it will. It's going to result in a lot of supply chain disruptions, because even in API manufacturing and excipients, we require a lot of these materials that come from different parts of the world.

DA: Are there any clear takeaways about TriRx's approach to quality that you'd want readers to remember?

JS: The thing that we do differently, which our customers and suppliers talk about is our alignment across the organization on what's important and what's not important. Everyone is committed to quality – it is part of our fundamental makeup. That alignment enables us to make decisions at lightspeed compared with everybody else. We can tell a customer that a product is not a good fit for us or is a great product and we'd love to help with it – in about 20 minutes.

DB: We can make and we do make decisions very quickly. Our clients always appreciate it and are amazed in many instances that we can do things so quickly. The final things I would like readers to know is that TriRx is committed to a quality systems approach to quality management and regulatory compliance, and quality/regulatory compliance is embedded in the fabric of our operating philosophy.

ABOUT THE AUTHORS

Jim Scandura
Co-founder, Director, Executive Vice President, and Chief Operations Officer
Jim Scandura has a wealth of pharmaceutical industry experience through projects with i-Solutions, a specialty life science consulting company. He has managed three major pharmaceutical manufacturing network change programs, three consent decree recovery efforts, over 30 manufacturing site audit and operational improvement efforts, the integration of a large R&D center and the direct management and integration of several manufacturing sites. Prior to TriRx, Mr. Scandura held senior roles at several major pharmaceutical companies, including Avara, Bristol Myers Squibb, GSK, Roche, Valeant, Patheon and Aptuit. Earlier in his career, he was Senior Vice President for Johnson Controls Inc. and, prior to that, served in the United States Navy Nuclear Submarine Service. He holds a B.S. in engineering from the University of the State of New York.

Donald Britt
EVP, Chief Quality & Regulatory Affairs Officer
Donald Britt has over 40 years of experience in the pharmaceutical industry, primarily in quality and regulatory affairs. Prior to TriRx, Mr. Britt held several senior quality positions, including Senior Vice President of Global Quality for Rhone Poulenc Rorer, Senior Vice President of Global Quality and EH&S for Aventis Pharma, Senior Vice President of Global Quality for Centocor Biologics, and Senior Vice President of Global Quality for Watson (Allergan). He has also held various positions of increasing responsibility within quality at GSK and, earlier, was Manufacturing Manager for Bayer Biologics. Mr. Britt began his pharmaceutical career working in the analytical laboratory at Baxter Travenol. He has a degree in biochemistry from the University of South Carolina.