900 Seconds At XenoTech

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Leading contract research organisation gains hundreds of hours in research time thanks to new QA method

Contract research organisations (CROs) have been growing at an impressive clip since the 1990s when the R&D efforts and needs of pharmaceutical companies started becoming increasingly more complex. Despite their ongoing focus on innovation, most pharmaceutical companies, regardless of size, have also had to bear the weight of increasing external cost pressures, contributing to the downsizing trend over the past five years. CROs have had to step in to not only allow companies to expand their R&D efforts beyond their in-house capabilities, but also to patch up gaps in competencies.

Indeed, CROs provide substantial global capacity to drug developers and have become a critical contributor to clinical trials activity. According to a 2009 study conducted by Business Insights, an independent market research firm, clinical trials conducted by CROs are completed up to 30% more quickly than those conducted in-house by pharmaceutical companies. The study notes that, two years ago, the total CRO market size was estimated at $20 billion and is expected to grow at an annual rate of 8.5% to reach $35 billion through 2015. These kinds of predictions reflect the ongoing growth opportunities for CROs, especially in the current economic climate. However, with more players entering the field, regulatory standards are bound to become more stringent worldwide. Successful CROs will be measured not by the amount of business they conduct, but by the quality assurance of their results.

XenoTech LLC - a Kansas-based CRO founded in 1994 and offering drug inhibition, enzyme induction, and drug metabolism studies for pharmaceutical, chemical, food, academic, and regulatory organisations in the United States, Japan, and Europe - realised the importance of quality assurance in its lab early on. Most of the studies performed by the company are governed by Good Laboratory Practices (GLP) standards to ensure data quality. For XenoTech, a high standard of data quality translated into, among other things, the regular verification of its automated liquid handling equipment. According to Steve Otradovec, XenoTech's Lab Automation Senior Scientist, the lab's automated liquid handlers are used primarily for sample preparation and incubation - the bulk of XenoTech's work.

"After purchasing our first liquid handler, we decided to verify it monthly - at a minimum - to maintain consistency with our verification standards for our manual pipettors," explained Otradovec. "At that point in time - this was about six years ago - it seemed like most liquid handling companies dismissed the need for routine verification, insisting that annual verification was sufficient. At XenoTech, we constantly strive to perform our work to the highest standard of quality and this demands a trustworthy assurance that our equipment is operating effectively. We can't put faith in mechanical equipment; we need evidence. We're also highly SOP-driven, and our robust SOP requires monthly validation of this equipment."

In 2006, XenoTech verified its liquid handlers gravimetrically using balances. Each liquid handling robot took four hours to validate.

"We knew that if we added more automated liquid handlers, we'd practically have to hire someone full-time to verify them," added Otradovec. "That's what drove us to find another method."

Fifteen minutes

As XenoTech set out to find alternatives that would minimise the time it took to validate its automated liquid handlers, it began to experiment with developing an in-house spectrophotometric method. As it strove to replace gravimetry in its lab, the company learned about Artel.

Based in Westbrook, Maine, Artel has pioneered liquid handling quality assurance worldwide. The Artel MVS (Multichannel Verification System) uses dual-dye ratiometric photometry to assess the precision (repeatability of volume transfer) and accuracy (closeness of transferred volume to target volume) for each tip of almost any multichannel pipetting device at volumes as low as 10 nL. Because measurement results are NIST-traceable, the MVS allows for direct comparison and measurement consistency between operators, methods and liquid handlers - regardless of make, model, manufacturer or location.

"When we heard about Artel, we realised that the MVS would allow us to do exactly what we'd been trying to and more," said Kammie Settle, Marketing Manager, XenoTech. "We're dispensing such low volumes, and everything has to be very accurate and precise to be repeatable and robust. Offering GLP contract services, we put a lot of emphasis on repeatable data. Samples have to be within a certain range. The more accurate our incubations are, the better our data are - we don't like to do repeat tests that use our time and resources ineffectively."

Keith Albert, PhD, Artel's Technical Marketing Manager, arrived at XenoTech with the MVS and proceeded to do an installation and operational qualification on site. To Otradovec's delight, Albert completed the installation in less than two days and proceeded to conduct a hands-on training for all technical staff.

Since Albert's visit in 2006, XenoTech went on to acquire additional automated liquid handlers to manage the increasing workflow. Using the MVS, the time it takes to accurately verify each robot was slashed significantly - from four hours down to 15 minutes.

Having experienced such dramatic time savings with its liquid handler verifications, the company started using the MVS to troubleshoot new scripts. According to Otradovec, XenoTech's use of the MVS goes beyond equipment verification since the system is able to mimic what a new script does ensuring that it's working correctly. For instance, when XenoTech builds a script for its automated liquid handlers, it can use the MVS to make sure that specific target volumes within different automated scripts are transferred with accuracy and precision, before implementing them.

Figure 1. Xenotech Research Scientist of R&D/Method Validation of Laboratory Automation, Robert T. Grbac, using the Artel MVS® to measure the accuracy and precision of his automated liquid handler.

Another time saving benefit of the MVS for XenoTech has been its ability to troubleshoot the company's liquid handling robots. "When we want to troubleshoot a liquid delivery, we can use the typical automation interface and deck set-up without the need to rearrange the deck for a gravimetric balance or an alternative software program," explained Otradovec. "The ability to test in real mode has enabled us to find liquid handler hardware problems that would have been unidentifiable using alternative gravimetric methods."

A booming future and time to invest in it

Twenty years ago, the role and business model for CROs used to be simple. Pharmaceutical companies were in charge of developing a new drug and taking it through clinical trials, and CROs handled outsourced work for the drug company, staffing a trial or analysing the data produced in the study.

However, with competition, financial pressures and looming patent expirations battering the pharmaceutical industry, drug companies are continuing to turn to outsourcing as a principal component of their new business models. While this has led to CRO growth, it's also leading companies like XenoTech to provide more than just outsourced work. "Our services go way beyond screening," noted Settle. "We specialise in regulatory submission studies, and provide our customers with enough information, going beyond mere technical data, so that they can make an informed decision on whether they should move forward with a compound's development, and what that next move might be."

With 250 customers in the pharmaceutical industry relying on XenoTech's studies at any given time, the company's focus on quality and high standards will likely continue to help set it apart from other CROs.

Many of the studies performed by XenoTech revolve around in vitro enzyme induction studies in human hepatocytes, which are conducted in accordance with FDA recommendations. The company's process involves treating cultured hepatocytes from three human livers for three consecutive days with three or more concentrations of drug candidates. These, among other studies conducted at XenoTech, have the important task of predicting metabolic pathways in humans' years before human clinical trials are approved, and can also be used to predict dangerous drug-to-drug interactions. This is no small feat, and quality assurance and control play an integral role in achieving it. By bringing the Artel MVS into its lab, and with its current population of liquid handlers, XenoTech has added 336 hours per month to the time it can spend focusing on developing ground-breaking studies that can help drug companies bring safer drugs to market faster.

New Diaphragm Valves Boost Performance

Alfa Laval's range of components and solutions for the biotech and pharmaceutical industries now includes a comprehensive selection of the Alfa Laval Unique diaphragm valves. They are configurable to meet most requirements, including aseptic conditions as well as sterile and ultra-hygienic processes. The unique design of the valves offers multiple benefits: longer diaphragm lifetime, increased uptime and lower installation and operating costs.

Reliability is essential in these industries, and the Unique Diaphragm Valve UltraPure continually delivers optimal performance. The modular design makes these valves perfect for a wide range of applications, and they can be combined in many configurations with different accessories and diaphragms. All valves in the range come with Alfa Laval's comprehensive documentation package.

The valve offers the highest possible quality throughout every component, including high-quality valve bodies with low delta-ferrite content and specified sulphur content as standard. Several valves are available in both block and forged versions; the latter provides a lightweight, cost-effective solution that is quick to heat up during heat sterilisation.

The Unique Diaphragm Valve UltraPure can be operated manually using a handle or automatically using a pneumatic actuator. Lightweight and compact, the actuator can be fitted with an extensive range of control and indication equipment. The actuator has a unique design that provides adjustments of spring pressure and makes it possible to alternate between different control functions. Adjustable spring pressure on the actuator and over-closure protection on the handle prolongs the lifetime of the diaphragm and increases uptime.

Horst Neuland, Chief Plant Engineer at Bayer HealthCare in Wuppertal, Germany, is positive to the Unique Diaphragm Valve UltraPure. The adjustable springs protect the diaphragms against overstress. "We don't have to stop fermentation processes as often to change the diaphragms on these valves, and the valves themselves last longer," explained Neuland. "This translates into minimal downtime, lower overall costs, increased productivity and higher profitability."

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