Bioanalytical Outsourcing Soars as Drugs Grow More Complex

CROs emerge versatile even as bioanalysis expands in scope. *This is the fifth of a nine-part series of articles addressing pharmaceutical outsourcing industry trends.*

SOMAN HARACHAND - CONTRIBUTING WRITER, CONTRACT PHARMA

Outsourcing in bioanalytical lab services is set for explosive growth in the coming years as the increasingly complex nature of modern-day therapeutics makes partnerships with expert contract research organizations (CROs) indispensable.

Large molecules, which are currently at the forefront of drug development, are developed through complex processes, often involving over a thousand steps.

"Protein drugs have increasingly become more complex. From humanized to fully human antibodies we now see more bi- and tri-specific antibodies, and other modified or truncated proteins. This leads to different assay requirements, especially for assays to characterize immunogenicity," says Radboud van Trigt, senior director of bioanalytical science, ICON Plc, a global CRO with headquarters in Dublin, Ireland.

Modalities are also more complex in the relatively new field of cell and gene therapies (CGTs) from a bioanalytical point of view. They often require multiple different assays on various platforms to understand their efficacy and safety. These can include flow cytometry and PCR-based methods and require the bioanalytical laboratory partner to offer a broad range of analytical technologies, according to van Trigt.

CGTs and mRNA approaches are among the new modalities CROs see a higher demand alongside a rising number of requests for biosimilar studies.

More and more large molecule drugs are nowadays quanti-

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fied using LC-MS/MS assays.

Some assays have the tendency to become more complex. In these cases, explains van Trigt, more method development time may be needed to understand the assays. An example is the growing need for high-sensitivity platforms to either measure the pharmacokinetics (PK) of very potent new drug modalities or biomarkers that would have otherwise been too low to quantify.

ICON aims to grow biomarker services together with ICON Central Laboratory Solutions so that they can use their combined strengths to offer "a versatile menu of services in this space."

BIOMARKERS FIRE UP DRUG DEVELOPMENT

Biomarkers are now in great demand as there is an increasing trend of integrating biomarkers in development and clinical practice to improve the selection of drug candidates and increase the speed of the development process.

"We are seeing an increase in requests for the assessment of the PK/PD relationships, and a particular growth in the biomarkers business, as customers try to establish a clear relationship between these PK/PD models and clinical efficacy. This should ultimately lead to faster approvals and fewer subjects required to complete a pivotal efficacy trial," says Manlio Bolla, senior director of bioanalysis at Syneos Health, a leading CRO head-quartered in Morrisville, NC.

Data derived from robust and reproducible bioanalytical assays form the foundation of all pharmaceutical marketing approval submissions to regulatory agencies.

With deep expertise in a broad range of therapeutic areas, Syneos Health receives many requests for drug-drug interaction studies, as well.

THE STEADY RISE OF BIOLOGICS

Considering the high level of testing required for the validation of the efficacy and safety of bio-based drugs, biopharmaceuticals will likely drive the growth of the global pharmaceutical analytical testing outsourcing market which is expected to reach $14.6 billion by 2030, expanding at a CAGR of 8.4%, as per the data by ReportLinker.

By year-end 2022, the number of biologic approvals outpaced that of small-molecule NME—a landmark in biologics' steady rise since the end of the twentieth century, show reports.

Newer modalities including bispecific antibodies, antibody–drug conjugates (ADCs), and CGTs accounted for about half of the bio drug approvals through the end of November 2022.

The small molecule therapeutics segment, which remains the biggest area, accounted for the largest revenue share of over 56% in 2021, according to a report by Grand View Research, a U.S.-based market research and consulting company.

Mechanisms of action of small molecule drugs too have changed over the years. A wider range of targets are now used for modern small molecule drugs, van Trigt points out.

Although North America holds the largest revenue share owing to the presence of a significant number of pharmaceutical companies in the region, Asia Pacific is anticipated to be the fastest-growing regional market due to the low-cost service offerings by third-party service providers in the region. To leverage the opportunities, many global CROs are expanding their base to these geographies. Recipharm, a leading global contract development and manufacturing organization (CDMO), which completed a new analytical laboratory at its facility in Bangalore, India to cater to the rising demand for the company's stand-alone analytical solutions in August 2021, is an example of this growing trend.

CROS: STAYING AHEAD OF THE CURVE

As CROs grow versatile in their service offerings, the bioanalytical labs outsourcing industry witnesses a massive shift of work. Studies indicate that there has been a surge in the externalization of bioanalytical activities from in-house laboratories to CROs.

According to van Trigt, there is a growing number of technology platforms utilized within bioanalytical laboratories. This means that the minimum critical mass needed to operate a bioanalytical laboratory has grown. The range of experts needed, both from a scientific and operational point of view, has also grown. Consequently, only larger companies can afford to have all this knowledge in-house.

ICON bioanalytical laboratories, which support a range of sponsor companies, collaborate closely with many academic institutions like the University of Groningen in the Netherlands to "stay ahead of the curve" meeting the needs of the industry.

Nearly every pharma and biotech company, including big firms running highly resourced labs, will outsource bioanalysis to CRO partners at some point in the development cycle.

This is because building an array of technology to provide analysis at different levels of sensitivity and specificity is expensive. So are full-time, permanent specialized personnel to ad-

dress needs that are most of the time temporary and variable.

"Pharma companies clearly see no interest in having immobilized capitals that are not exploited to their capacity. CROs can often provide these services more efficiently," says Bolla of Syneos Health, which runs three labs—two in North America and one in Europe—catering to the needs of companies in terms of bioanalysis and biomarkers globally.

Some sponsors may not have the resources or time necessary to onboard the expertise needed to support regulated bioanalysis. So, they can't help but outsource.

Notably, emerging biopharma companies contributed to a record 65% of the molecules in the R&D pipeline in 2021, shows IQVIA Institute for Human Data Science Report published in 2022.

RESHAPING RELATIONS

Even as bioanalysis outsourcing is continuing to increase in terms of volume and scope, the association between sponsoring companies and their partnering CROs is also changing.

Two decades ago, bioanalytical CROs were mainly providing transactional services wherein an existing method was transferred and the CRO was used as a pair of extra hands to run the analytical execution. This has gradually evolved, notes van Trigt, into a situation where scientific advice from the CRO is now requested for many projects.

The technical and experience strengths of the providing CROs now often compare with—or even outweigh—those of the sponsors. "The number of different modalities CROs have at our disposal is usually greater than a typical pharma laboratory would have," says von Trigt. Although the pharmaceutical company will have all the details about their drug and its mechanism of action, they may not always oversee the bioanalytical challenges and regulatory aspects of the requested methods.

CROs are becoming more than just an outsourcing partner focused on transactional activities and are increasingly being viewed as long-term strategic partners.

FASTER ANALYSIS, SMARTER DATA

Another driver for increased outsourcing of analytical testing is short turnaround times.

"Customers desire rapid response and prefer broad capabilities to provide services as a one-stop-shop," says Bolla. Syneos Health runs Syneos One, a dedicated interdisciplinary team providing end-to-end services for the seamless delivery of asset development solutions.

With increased emphasis on automation or automation-assisted workflows, the service providers aim to accelerate the process and the proportionate cost efficiencies. Automated laboratory instrumentation interfaced with flexible LIMS systems enables labs to deliver smarter data faster so that development decisions can be made at earlier points in time.

Complex structures having large molecular weights make bioanalytical testing of large molecules a challenging task as traditional techniques used for classical drugs are not adaptable. The CROs are addressing the industry need by adding advanced techniques such as ligand binding assays (LBA), Maldi-TOF-MS, size exclusion affinity chromatography, high-resolution mass spectrometry (HRMS) etc. And large molecule testing is mostly outsourced.

ICON has doubled capacity and added new technologies that are highly automated, including the Gyrolab platform for supporting pharmacokinetic assessments of protein therapeutics.

"We have strong ambitions for continued growth across all of our services, whilst investing in the latest technologies, and expanding our capabilities in areas such as PCR and ELISpot," says von Trigt. ICON has three bioanalytical laboratories in Europe and the U.S.

In 2021, ICON acquired PRA Health Sciences, one of the world's leading global CROs by revenue, providing outsourced clinical development and data solution services in a $12 billion deal. ICON employed approximately 41,100 employees in 111 locations in 53 countries as of December 31, 2022.

REGULARLY CHANGING REGULATIONS

The demand for extensive and precise large-molecule bioanalytical testing services is also boosted by an increasingly stringent regulatory landscape.

Experts see the demand for bioanalytical testing services to advance further in the coming days as the legislation for *in-vivo* and *in-vitro* tests is changing with increased complexities. The need for electrophoresis, titrimetric assays, electrochemical assays, and immunoassays is rising with the growing demand for combination medication, biosimilars, and other novel drugs.

Considering its critical nature in establishing the safety and efficacy of the drug, bioanalytical testing of study samples is a highly regulated process. And the regulatory landscape around bioanalyses changes regularly.

Frequent auditing by global regulatory agencies promotes higher confidence and demonstrable assurances of data accuracy while helping CROs enhance their understanding of regulatory practices worldwide.

Ultimately, what matters most is quality. Sponsors look for labs from where they can "obtain quality results that will be accepted by regulatory agencies around the world," says Syneos' Bolla. **CP**

Soman Harachand is a pharmaceutical journalist based in Mumbai and a regular contributor to Contract Pharma. He can be reached at harachand@gmail.com.