A sparC of Innovation

COVANCE®

Patients can’t wait.
And neither can we.

Author Lewis Carroll famously said, “If you don’t know where you are going, any road will get you there.” I believe that, at last, as an industry we’re beginning to form a shared vision of where we’re going. We’re untethering ourselves from the here and now, looking past the way we’ve always done it, and tackling challenges with a clean slate and an open mind.

As I look to the future of life sciences, I see incredible scientific advances in human health. But I also see innovation moving beyond the bench to the business of bringing a drug or device to market. That journey is being transformed in unique ways delivering life-saving products and health technologies to patients faster.

We are delivering cohesive development plans that begin with the end in mind… in other words with the patient at the forefront of all design and operational decisions. We are pursuing strategies that are informed by real-world data and processes streamlined by automation and overwhelming volumes of data tamed by Machine Learning (ML). Together we can transform trials.

In the following pages, you will see this, too. At Covance, we’ve embraced innovation to turn this aspirational future into today’s reality. With the power of LabCorp and Covance combined, we’re 50,000+ strong and brimming with new approaches to help you achieve your scientific and commercial goals. This is but a glimpse into the bold new world we’ve entered and I invite you to join in on our innovation efforts via sparC.

Thanks for all that you do every day.

Connect here with us if you would like to start the conversation around any of the featured solutions.

Sincerely,

Paul Kirchgraber, MD
CEO, Covance

solutions **p**rogressing **a**nd **r**evolutionizing **C**are

Welcome to **sparC Magazine**, which is dedicated to highlighting our **S**olutions **P**rogressing **a**nd **R**evolutionizing **C**are initiative.

How mobile health, local sample collections and virtual models are redefining where clinical trials happen

We live in an era where there is an expectation of immediate results. We connect with other people and with companies via the web, mobile apps, internet chats – all centered on getting something done conveniently, right now.

That same expectation is also at the crux of today's biggest challenge in clinical trials – where inconvenience to prospective trial participants is disrupting a sponsor's ability to recruit and retain trial patients.

According to Bola Oyegunwa, Vice President and Global Head of Hybrid and Virtual trials: "Sponsors all too often struggle to find enough of the right patients for their trials. Clinical trials are becoming more complex and require more data-driven models for targeting prospective participants. But in the end, it comes down to the hurdle of inconvenience for patients to participate."

A survey conducted by Covance of more than 600 U.S. trial participants revealed the most significant barrier to trial enrollment is the burden of travel to investigator sites. The survey showed that the average investigator site in the U.S. is more than 25 miles from a patient's home, which can impose a significant challenge on participants and their caregivers. In Europe, the distance is reported to be even greater, at an average of around 30 miles.

To increase participation in clinical trials, Covance is developing a range of innovative trial models ranging from hybrid trials – where some travel to sites is replaced with different ways of performing these visits, to fully virtual trials – where trips to investigator sites are eliminated altogether.

When a patient's physical presence is required for certain limited procedures, such as a blood draw, Covance offers a unique model that reduces the average travel distance, thus reducing the burden on the patient.

Run by parent company LabCorp, a nationwide network of more than 1,800 U.S.-based Patient Service Centers (PSCs) is available. The PSCs are staffed by highly trained phlebotomists with diverse sample collection and biometrics capabilities. Based on the survey of trial participants, there is a PSC within an average of three miles of a patient's home, which is a significant decrease from the average distance of 25 miles to a traditional investigator site.

"The continuous data from mHealth devices gives a much richer picture of what is going on when compared to taking a few isolated data points throughout the day."

Combining PSCs with mobile health (mHealth) technology, the convenience factor is improved even further. mHealth solutions may deliver new technology for patients to provide consent online or through an app (eConsent), speeding their path towards enrollment by improving accessibility and simplifying the process for trial participants.

What's more, mHealth enables a clinical trial's data to be collected remotely, and shared with trial management personnel in real time. mHealth options are often easier to use and less invasive than their traditional counterparts.

For example, should a trial participant require frequent glucose monitoring, mHealth capabilities could mean the patient no longer needs to conduct several finger pricks throughout the day. Instead, a device patch

An Increasingly Growing Challenge

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Traditional Trial Design

Average distance a patient needs to travel to a trial's site:
>25 miles from their home

Patient Identification

Consent, Screening & Enrollment

Investigational Product & Supplies

Study Visits & Data Collection

Our Covance Response

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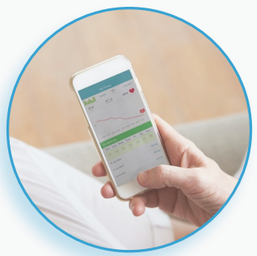


Study Visits & Data Collection

containing a continuous glucose monitor may be worn to constantly record the required data, report back to the trial operators, and alert the patient if blood sugar levels become dangerously high or low.

When it comes to documentation, manual collection of patient-reported outcomes, traditionally done via paper diaries or surveys, may be replaced with mobile apps for electronically collecting patient-reported outcomes (ePROs). This innovation removes the need for patients to document issues by hand, and eliminates the need to carry paper diaries. It may also make it easier to collect information throughout the day and improve capture of critical observations by the patient

From a sponsor's perspective, mHealth helps researchers build an increasingly stronger dataset and improve communication with trial patients, leading to richer insights and a care program better suited to the final target patient.

According to Oyegunwa: "The continuous data from mHealth devices gives a much richer picture of what is going on when compared to taking a few isolated data points throughout the day.

"Devices such as an electrocardiograph or a respirometer can be used at home or at work by the patient, eliminating the need to visit an investigator site and making life so much more convenient for the patient. That convenience factor can be the ultimate driver for participation."

So, will sponsors adopt virtual means? A 2017 survey found that 94% of the biopharmaceutical companies that participated were looking to increase their use of mobile health in the future, with 55% of North American firms "very likely" to increase their use by 2019. This means the probability of your next clinical trial being driven by some form of virtual ingenuity is highly likely.

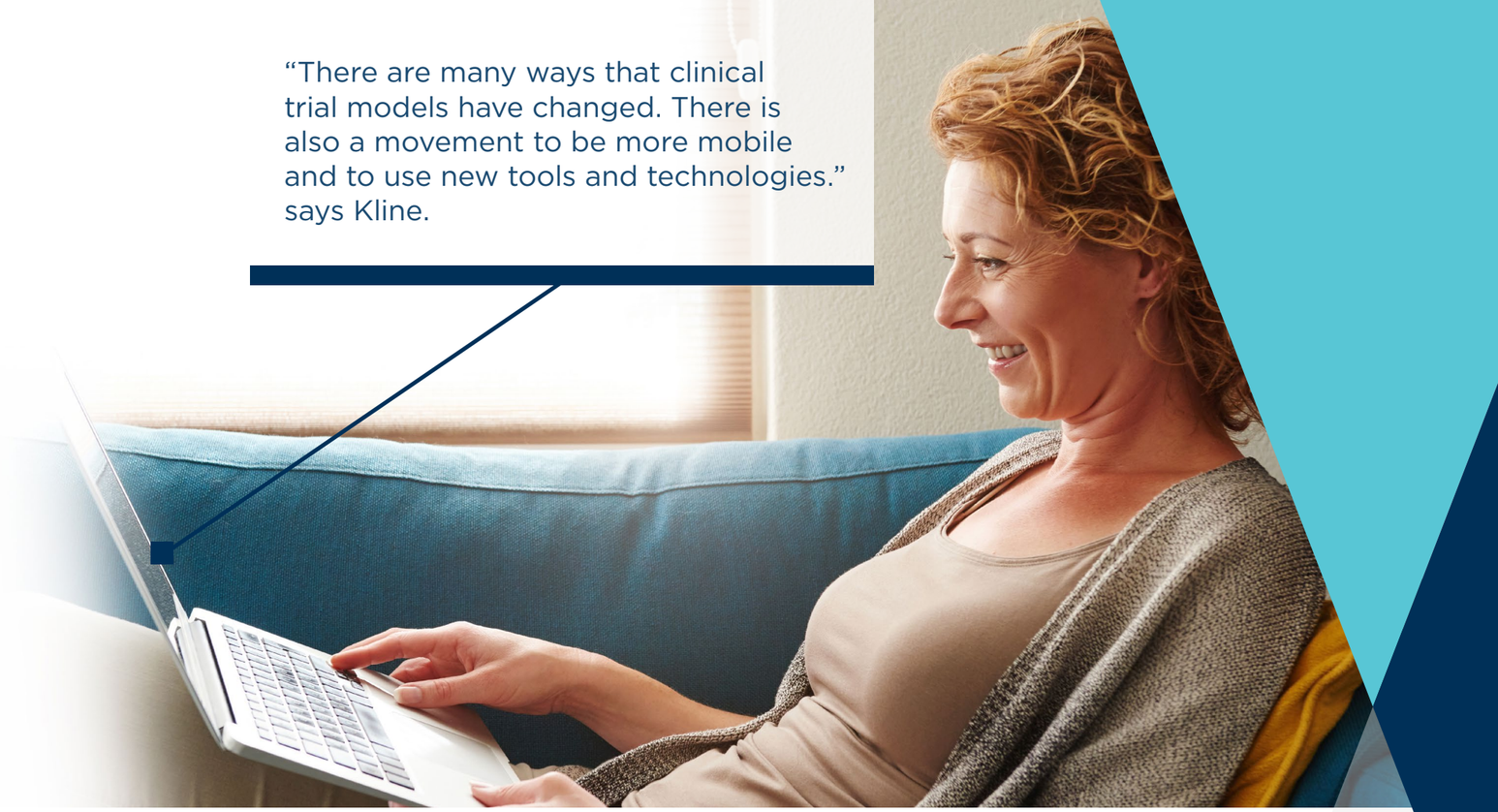
Will that trial entail mHealth technology, conveniently-positioned PSCs or some other virtual innovation? Quite possibly. While fully virtual trials are relatively rare, hybrid trials are becoming increasingly common, using traditional tried and true methodology alongside elements from the new, virtual toolbox.

Hybrid trials are the sweet spot for the moment. With the ability to accelerate enrollment and improve patient retention through relatively low-risk means, they can help speed clinical trial completion while minimizing disruption in patients' lives.

"The bottom line: convenience matters. A lot," says Oyegunwa. "Moving the trial beyond the traditional investigator site to a more patient-centric approach will ultimately eliminate participation barriers – making the trial more accessible to the patient, while generating a richer and more insightful data set."

It's a win-win for the patient and the sponsor.

"The bottom line: convenience matters. A lot. Moving the trial beyond the traditional investigator site to a more patient-centric approach will ultimately eliminate participation barriers – making the trial more accessible to the patient, while generating a richer and more insightful data set." says Oyegunwa.



"There are many ways that clinical trial models have changed. There is also a movement to be more mobile and to use new tools and technologies." says Kline.

How patient centricity is enabling the reality of virtual trials and mHealth

It's a well-cited fact that the greatest challenge facing clinical trials today is patient recruitment and retention.

Low rates of participation are an industry-wide problem, often stopping a study before it's even begun and "slamming the brakes" on essential medical progress. However, it seems a solution may, in some part, be simple.

According to Greg Kline, Executive Director of Patient and Market Intelligence, in the mission to make trials more efficient and cost effective, the patient voice is rarely prioritized and all too often overlooked.

"Insights from over 65,000 patients show that the number one reason a potential participant will not enroll in a trial is convenience," says Kline.

"Anything that we can do to be more patient-accommodating and increase the convenience factor for participants could change the face of the industry."

And changing the face of the industry is exactly what Covance is on a mission to do. For the global firm, this means leveraging daily access to millions of patients via parent company LabCorp, and combining it with the company's own patient intelligence infrastructure consisting of insights from over 30 indications and 20 different countries, to decode the answer.

According to Kline: "From anonymized, aggregated laboratory results of approximately 150 million individuals in the LabCorp database plus our patient intelligence tool, we can see, for example, that there are a specific number of people in a particular area with certain results which are indicative of a particular disease."

"We can also target the more than 65,000 patients that we have in our intelligence tool and add their voice to the mix as well. We are then able to hone in to see what patients within a given radius think about joining a trial and the elements most likely to drive them to participate."

"This combination of LabCorp data and patient insight data is what we're finding to be most powerful."

The result? The ability to craft stronger trial models that address patient preferences, with the goal of enhancing patient convenience and recruitment and retention rates.

For example, research has found that the average distance between a clinical trial patient and an investigator site is more than 25 miles. It stands to reason, then, that reducing this distance will go some way to increasing enrolment.

By leveraging LabCorp's more than 1,500 PSCs, access to clinical trial patients could be as little as five miles away; a seemingly small reduction in distance that can make a huge difference to a participant and how disrupted their day-to-day life is during a trial.

While the improved proximity to a PSC is a significant factor in increasing a study's convenience factor, it's not the only way the company is improving patient centricity.

"There are many ways that clinical trial models have changed. There is also a movement to be more mobile and to use new tools and technologies." says Kline.

Virtual trials and mobile health (mHealth) has gained an upsurge of interest in recent years thanks to the advent of smartphones and wearable technologies. These advances can help to reduce the frequency of investigator site visits and monitor key study end-points throughout the day through the use of devices such as smart patches. When it comes to elevating patient centricity, are virtual trials the most convenient of them all?

Perhaps. But in the meantime, Kline believes we can make significant strides by truly listening to patients. "Everyone wins when you're learning and listening. Convenience is more than just having easy access to an investigator site; it's about building a protocol that is designed to be convenient to the patient, with the patient preferences embedded into it.

"We have studied many different patient populations and the idea that people will go anywhere for a clinical trial is a fallacy. People have daily responsibilities, commitments and costs to consider. But we need to begin to think about the convenience of our patients and develop new and different ways to enhance the trial model to match."

"What's truly exciting is that the unique infrastructure of Covance and LabCorp together now allows us to truly bring our clients something different and innovative in this space – to transform the future of clinical trials with an unprecedented level of patient visibility," concludes Kline.

Programmatic approach:
An innovative model for drug development that delivers speed and flexibility from candidate to proof of concept

It is estimated that 70-80% of biotech firms still follow a study-by-study approach for their drug development program, often driven by investor requirements and cash flow limitations.

It is a transactional model that typically involves investments being awarded based on milestone achievements which, in turn, causes sponsors to select development partners to conduct studies on an “as-funded” basis.

While some biotechs see this as a prudent way to manage their program, it comes with a range of disadvantages from a risk perspective. For example, developers might experience an increase in downtime between studies due to the need for knowledge transfer between teams or vendors, as well as increases in the time and cost of data handling and sharing.

They also greatly expand their vendor management tasks, spending additional time and resources to research and select vendors and negotiate terms, risking duplication of efforts, and delays between nonclinical and clinical phases.

However, there is a clearer approach that allows developers to prospectively map out the journey of their product, providing full line-of-sight to scope, timelines and cost, as well as enabling a plan of action for risk management.

This programmatic model allows sponsors to begin development with the end goal in mind, replacing a just-in-time approach with a strategic programmatic outsourcing model that can better inform, convince and inspire stakeholders and all involved parties.

Better still, it has been proven to save up to 30% of development time as the product moves through preclinical and into early clinical phases, while enabling better risk mitigation, stakeholder communications and opportunity for delivering on investor expectations.

Mitigating risk

According to Michelle Scott, Vice President and Head, Biotech Development Solutions: “There are multiple factors why biotechs benefit greatly from a programmatic approach. They can achieve everything they need in one plan, while also removing the need to manage multiple partners.”

Some may perceive the “all under one roof” approach to be riskier than a piecemeal model, but this is not the reality, according to Scott. Risk is actually reduced by having one provider with line-of-sight to the complete plan.

“Understanding all of the different aspects and how they fit together enables the client to generate value straight away, even if the product is very early in development.”

“I spend a lot of time talking to investors, and a key element they like about Covance is the quality of the upfront strategy and subsequent study work that helps de-risk the project. It makes the biotech more investable, and from a pharma partner point of view, Covance’s model provides reassurance and confidence,” explains Scott.

When it comes to aligning funding rounds to a biotech’s program, Scott suggests it’s still possible to adopt a holistic approach, because developers are not required to pay for everything at once. In fact, a programmatic approach may even help biotechs to reduce their costs and better deliver on milestones, creating savings in time and direct expenses simply by not having to use already limited resources to continuously find and manage multiple CROs.

“Understanding all of the different aspects and how they fit together enables the client to generate value straight away, even if the product is very early in development.”

Scientific and data continuity

With a programmatic approach, necessary advisers are at hand. Scott explains, “We can provide clinical, biomarker and regulatory experts, or someone who understands structures of molecules, or who can explain the value of their molecule, for example, because they’re all at Covance, giving clients the ability to save both time and money.”

Another significant benefit is the continuity provided when it comes to data management. Each time a new party is introduced into the development process, there is the potential for gaps in knowledge to emerge, or for data to be duplicated or become inconsistent. When a biotech chooses one provider to see them through all phases, a continuity of science can be achieved, and developers can be confident in the accuracy of their data.

“Drug development is never linear,” says Scott. “There are always bumps in the road, and biotechs need to continuously adapt, so it’s important to be as integrated as possible to be ready to pivot.

“Our programmatic approach is led by one team that can bring in specialists as needed from across the business. In fact, Covance is the only CRO that can provide this level of continuity from nonclinical all the way through to clinical, and even on to market,” concludes Scott.

For more information about how you can save up to 30% on your drug development timelines, visit here.

Finding commercial success by integrating development, regulatory and market access strategies from the get-go

When bringing a drug to market, there is a range of scientific, clinical, regulatory and market access challenges that pharmaceutical and biotechnology companies face.

All too often, clinical development plans outline the path to gain regulatory approvals, but may not include a commercial strategy for maximizing market access once they get there, for example, with product adoption and use. This gap has led to marketed products that don't maximize their potential return on investment.

Creating a comprehensive development plan upfront – one that considers all aspects of the road to market, including identifying and addressing potential obstacles – helps the navigation of acceptable regulatory and commercial paths. Depending on the data, a successful clinical development plan can increase the possibility for regulatory approval, as well as commercial success once the product is on the market.

"The comprehensive development plan is the backbone of drug development," says Beatriz Rocha, MD, PhD, Vice President and Head Global Regulatory Affairs and Strategic Product Development Consulting.

"You have to ensure that the studies conducted will be sufficient to support the filing of the Market Application on your target indication, and support commercialization in the targeted world regions."

In other words, by clearly defining your destination at the very beginning, using a target product profile, you can more precisely define the plan to get there.

"As part of the clinical development plan, sponsors should define the market strategy. This means clearly identifying what payers and prescribers are looking for in the specific indication," explains Rocha.

This is a continuous process that can start as soon as proof of concept is achieved, and should be revisited as evidence on the product's safety and efficacy profile is accumulated throughout Phase II and Phase III.

A road map for success

A comprehensive drug development strategy – the road map for taking a product from a novel compound in the lab to a marketed drug product – is a key component of any sponsor's toolkit. Effectively implementing this plan can help reduce costs, improve efficiency and shorten development timelines.

According to Rocha: "When short and long-term market access goals are considered at the outset of a program and implemented throughout development, sponsors can more easily decide what development activities are most essential for reaching the ultimate goal, and plan the program accordingly.

"As part of the clinical development plan, sponsors should define the market strategy"

"A thoughtful development strategy can increase business efficiency and decrease timelines because it drives a sponsor's attention to those activities or studies that support their final commercial goal, reducing expenses and increasing focus on the critical studies."

"Once reaching initial regulatory approval, sponsors have already incorporated components into their plan that will enable payer and prescriber decision-making, as well as how to take the product into the market more rapidly."

An early, comprehensive review and analysis of the current and projected competitive market landscape for the intended patient population, is critical. Careful consideration should be given to the effectiveness, side effects, costs, insurance coverage and overall satisfaction with existing competitive drug products. Health technology agency expectations must also be factored in.

Based on such initial market research, sponsors can decide how best to differentiate their product from competitors and estimate its economic value, thus helping to improve its success in the market.

Setting sponsors up for success

Creating comprehensive drug development and commercial market access plans side-by-side is a smart move. To get the most out of both plans, many sponsors turn to CROs for help.

According to Rocha: "Clients can discuss their regulatory, clinical and market access strategies simultaneously with Covance, to gain an integrated approach to product development. This unique model provides a distinct advantage for our clients."

Paul Rothenberg, MD, PhD, Executive Director, Clinical Development Strategy, agrees: "When clients work with CROs to perform their clinical trials in a piecemeal fashion, they can short-change their long-term goals.

"Leveraging specialists with deep drug development experience that combines regulatory, clinical and market access disciplines can be a game changer for sponsors. They are able to devise comprehensive plans that integrate all strategies into one to seamlessly accomplish all their goals."

"There are many hurdles that a program faces when commercial and regulatory strategies do not go hand-in-hand, but Covance sponsors who engage in this model of planning are exceedingly well equipped to walk through those challenges more easily and to improve their ultimate chances of success in the marketplace."

AI and Automation: Transforming product and safety vigilance data into smart, personalized insights

Patients are using powerful drugs and medical devices, which are extremely efficient at enhancing and saving lives, but can come with complicated side effects.

Jerome Premmereur, MD, Vice President of Patient Safety Solutions says: “Monitoring the risk-benefit ratio of medical products is critical, yet the complexity of patient safety is becoming increasingly difficult to navigate due to the extremely large database sizes.”

Organizations developing new drugs or devices often outsource their clinical trials to one or more clinical research organizations (CROs) to manage the process, including product vigilance (or patient safety) activities. When multiple CROs are used, safety data may be stored, reviewed and reported separately by study and then manually aggregated at product level which is required by health authorities.

Sponsors then face the added challenge of integrating this data into a single database, yet they may not be adequately equipped in-house (people, skillset and technology) to do so. The inability to effectively review safety data at aggregate level as reports are made can lead to delays in NDA submissions or even failure to obtain marketing authorization.

“Automation adds value on two levels. One is in safety operations, where the sources of data are increasing year on year.”

“Safety data transition is essential at all stages of the product life cycle, especially during the clinical trial and even more so during the post-marketing phase, when processes, systems and technology become critical,” says Premmereur.

“Once a product goes to market, the complexities and regulatory mandates associated with product vigilance operations increase exponentially, along with the amount of data that is generated.”

Sponsors today seek better ways to bring high-quality products to market, while also managing and turning the significant amount of data that’s produced into intelligence.

“By closing the gap and transforming product vigilance output to deliver more personalized care through advanced analytics techniques, we can better understand the benefit-risk ratio of a product and how it may impact the specific profile of an individual receiving treatment,” explains Premmereur.

“To achieve this, the industry is increasingly turning to automation and artificial intelligence for the answer.”

Big data

Big data has enabled healthcare to process and analyze massive amounts of data and use it to improve the quality, efficiency and costs of healthcare along with a reduction in medical errors.

For pharma, it is aiding in the design of better treatment strategies in the march toward precision and personalized medicine, and for devices to integrate machine learning and predictive analytics to pave the way for smart devices and medical machinery that could diagnose and interpret results.

The practice of pharmacovigilance and post-market surveillance has not gone untouched by the ongoing digital revolution of the medical industry. Big data systems provide new mechanisms to monitor such things as signal detection, Individual Case Safety Report (ICSR) comparisons and adverse event reporting patterns.

Medical safety data repositories – such as the World Health Organization's (WHO) VigiBase, the European Medicines Agency's (EMA) EudraVigilance database and the Food and Drug Administration's (FDA) Adverse Event Reporting System – are expanding, with millions submitting reports annually.

According to Dinesh Kasthuril, Global Client Director: "Automation adds value on two levels. One is in safety operations, where the sources of data are increasing year on year."

This means a safety case processing operation now has to deal with increasing amounts of data, with an estimated growth rate of about 15% per year, with roughly the same amount of resources.

"Here's where automation can really help. By increasing the efficiency of the overall system of the organization, sponsor teams can focus on the value-added activities that are more medically relevant and have a higher impact on patient safety," explains Kasthuril.

The second area where automation can have an impact is in its ability to look across available data to identify and even predict potential signals. "Here, it is not so much about increasing efficiency, but rather employing artificial intelligence (AI) and machine learning to detect patterns across multiple patients that may take humans a longer time to recognize," says Kasthuril.

Smart systems

In recent years, we have seen the variety and size of safety data sources grow significantly. This shift requires enhanced technology solutions as a key enabler in patient safety operations.

But harnessing the benefits these tools have to deliver patient safety and personalized medicine has not been an easy path. "At the moment, sponsor organizations are struggling with how to choose and implement the infrastructure necessary to handle these technological developments, despite the fact that they will ultimately help increase productivity and enable them to flag or detect safety signals earlier," says Premmereur.

To enable clients to gain the full benefits of automation and AI in their product vigilance efforts, Covance helps organizations implement and utilize new technology, creating smart systems within databases to capture the complexity of the drug or device development continuum.

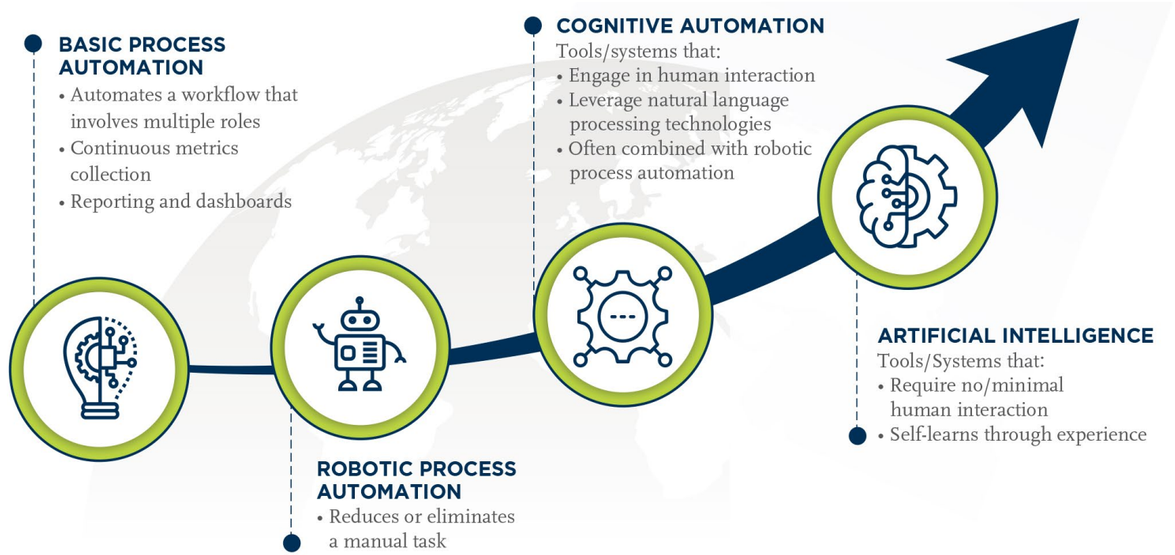
What's more, when clients outsource their clinical trial and post-marketing patient safety efforts to Covance, they can do so with confidence that it is managed by safety data specialists from under one standardized system. This way, all product data is seamlessly consolidated and analyzed as it is reported with ease while setting conditions to readily flag safety issues.

According to Kasthuril: "The entrance of AI and other automation developments signal a fundamental shift in how safety departments operate; however, we don't predict this to completely replace humans."

"Pharmacovigilance and post-market device surveillance departments of tomorrow will still require specialized teams that use medical and quantitative knowledge to provide safety solutions, aided or augmented by automation for optimal impact on patient safety."

Covance Automation Roapmap

At Covance, we understand the benefits that automation tools offer and how our clients can take advantage of them. Safety automation tools range from basic to robotic process automation (RPA), to cognitive and AI, offering a wide variety of technology solutions that can be utilized to drive operational efficiencies across the safety continuum.



Getting personal: How precision medicine is shaping the future of healthcare

Many people take for granted that the medication they have been prescribed by their physician will adequately treat or cure their ailment. Yet the reality is that a large number of the drugs prescribed come with a surprisingly low success rate.

According to analysis[1] by Nicholas J. Schork, PhD and Director of Bioinformatics and Biostatistics at the Scripps Translational Science Institute, some of the highest-grossing drugs in the U.S. help as few as 1 in 25 patients. Standard practice includes treatments given based on a physician's experience with similar patients, meaning medications are prescribed for a "typical patient" with the disease or medical condition.

But not all disease is homogeneous. The more we learn about disease biology, like tumor characteristics in oncology and the genetic components of rare diseases, the better we understand why single-target treatments can fail.

Hope for a solution has arisen with the development and evolution of the principles of precision medicine, where innovations are making therapeutic breakthroughs possible on a patient-specific basis.

Through precision medicine, a range of new technological advancements are helping to improve our understanding of diseases and changing the way physicians diagnose and treat. The result is more precise and powerful healthcare that is customized to the individual.

"In the last couple of decades, we've gone from a one-size-fits-all approach to a targeted one based upon the biology of disease and identification of the specific therapeutic target within that disease state," says Dr. Steve Anderson, Chief Scientific Officer.

"In areas like oncology or rare diseases, highly personalized therapeutic approaches are rapidly becoming a reality."

[1]Schork, N. (2015). "Personalized medicine: Time for one-person trials." *Nature*, Vol 520: 609-612

Navigating the development cycle

The quest for personalized care for each patient means providing the right drug to the right patient at the right time. Achieving a tailored therapy is not a simple process, but breakthroughs in developing precision medicines are making dramatic in-roads.

"In areas like oncology or rare diseases, highly personalized therapeutic approaches are rapidly becoming a reality."

In the last few years alone, precision medicines based on cell and gene therapies have emerged and are predicted to grow significantly. One indicator is from regulatory agencies such as the Food and Drug Administration (FDA), that announced an increase in the number of clinical reviewers to assess and help approve an expected ten to 20 such therapies per year by 2025. Global financing for precision medicine also rose by 64% to more than $17B USD in 2018.

Investment and research is clearly beneficial to providing improved medicines on a personalized basis, with highly specialized capabilities needed at every stage of the process.

According to Anderson: "As we look at the development of these novel therapies, it is becoming a very highly competitive field and there are numerous expedited regulatory approval pathways, so moving quickly though the drug development cycle to ensure success is essential."

"This means the ability to transition quickly from nonclinical into clinical development and remove as much whitespace as possible is critical. During development, looking ahead to the post-approval phase and understanding how to differentiate is also very important. Having that forward-thinking mind-set and perspective from a full-service provider is a huge benefit to sponsors."

"Clients choose Covance because we are a full-service CRO, with specialization in precision medicine," continues Anderson. "We can work with sponsors through all phases of development to transition quickly between these phases, such as from preclinical to clinical, to save client's time."

"In developing the appropriate nonclinical models, we can help sponsors understand the therapeutic candidate's mechanism of action and establish the potential for efficacy and toxicity in humans prior to clinical studies."

"For lab testing, we can work with sponsors in screening patients for the appropriate biomarkers to stratify patient populations and establish inclusion criteria in clinical studies. Moreover, in support of innovative clinical development programs, we have the ability to help with trial design and adapt the design as the study progresses."

"When there is a biomarker that proves critical to establishing whether the therapy will be effective in patients, Covance can support the co-development potentially leading to a companion diagnostic in collaboration with our parent company, LabCorp, making that diagnostic commercially available at launch."

Putting the patient first

Trial design in precision medicine creates a fresh set of challenges for sponsors already adapting to the evolving and sometimes region-specific regulations and tightening of budgets.

"Sponsors must manage the relationship between all stakeholders in the delivery of precision medicines."

Precision medicine trials must focus on smaller, targeted populations, while remaining flexible in design. A sponsor may start with one hypothesis, often driven by a biomarker strategy to identify patient cohorts, and need to adapt that design as they move through the development cycle.

Another significant challenge for some precision medicines is the high upfront cost, especially for cell and gene therapies that are potentially single-dose, curative treatments. However, Anderson predicts that prices are likely to fall as the industry develops manufacturing efficiencies, streamlines development and approval pathways, and competition increases.

"Sponsors must manage the relationship between all stakeholders in the delivery of precision medicines. They must work with payers determining coverage for the therapeutics or diagnostics, diagnostic developers, regulatory agencies and so on."

"This collaborative spirit of all impacted stakeholders finding the right path forward helps to balance the individual benefit with the broader cost to the healthcare system. Most importantly, a patient whose disease characteristics and unique genetic makeup are taken into account has a better likelihood for response to today's innovative medicines."

Functional Service Providers: A flexible trial staffing model that's capable of taking on biomarker data management

As large pharma, biotech and medical device organizations feel the economic pinch of escalating costs, stricter regulations and fiercer competition, many are seeking new ways to cut the costs of development in the face of decreasing margins.

One of the largest costs to address is staffing, including the cost of attracting, hiring and training personnel.

For clinical trials, two common trial management approaches have been employed over the years. One approach involves running the entire trial internally and outsourcing only specialized parts of the trial (such as lab testing work or investigational product supply). On the other end of the spectrum is the use of Contract Research Organizations (CROs) to fully outsource a complete trial.

However, a sponsor's desire to maintain a high degree of control over clinical trials without being responsible for directly staffing each individual function, drives a third approach that uses vendors as Functional Service Providers (FSPs).

This is where specific parts or functions of a trial, such as clinical project management, clinical research associate teams, data management, or biostatistics and statistical programming functions, are contracted as a scalable service and reduced or discontinued when the need has passed.

FSP is a trending and innovative staffing model that moves with the ebb and flow of an organization's innovation pipeline. It can materialize in many forms, from individual specialists to functional departments, depending on the sponsor or portfolio requirements. It can manifest as a resource-driven billing model or be designed around unit deliverables, or a hybrid of both approaches.

By outsourcing tasks by function or department, organizations boost operational efficiency and flexibility, thus giving managers the time to focus on their core mission. The FSP model also enables the sponsor to retain control over trial management in a fully flexible and scalable way.

Other benefits to FSPs include a reduced employment burden such as attracting and hiring talent, termination of employees and day-to-day staff management, while providing sound integration with the existing functions of the company.

So, can the same benefits of the FSP model for clinical trials be realized on the laboratory data management side?

As clinical studies have become more complex, we have replaced the need for sponsors to directly oversee all of these areas, with a specialized outsourced role delivering trained specialists who have a strong understanding of lab data.

With this process, sponsors get cleaner data, faster.

Cleaner data, faster

A growing feeling among sponsors suggests that labs should evolve with the clinical side of individual studies and provide fast resolutions to queries and urgent data management tasks, such as laboratory specialty data reporting.

"As clinical studies have become more complex, we have replaced the need for sponsors to directly oversee all of these areas, with a specialized outsourced role delivering trained specialists who have a strong understanding of lab data."

To answer the call, Covance launched Lab FSPx in August 2019. Lab FSPx is a laboratory data management solution that expands the Covance FSPx portfolio, complementing its clinical operations, clinical data management, medical writing, biostatistics and post-market vigilance capabilities. Lab FSPx is a highly focused service that draws from the unique combination of laboratory and data management expertise across the Covance organization.

According to Manish Soman, Senior Vice President FSPx, Safety and Regulatory: "Historically, sponsor data managers have been responsible for lab data, along with clinical data and all types of external data."

"As clinical studies have become more complex, we have replaced the need for sponsors to directly oversee all of these areas, with a specialized outsourced role delivering trained specialists who have a strong understanding of lab data. With this process, sponsors get cleaner data, faster."

"Covance has delivered an FSP model for 30 years, providing dedicated resources that are either remote or embedded as an extension of a sponsor's internal staff. Currently, 96 different functional relationships exist, each addressing a client's required specialized skillsets."

"Over the past four years, we developed a specialized role that is now offered through our new Lab FSPx that focuses on external lab data and the variety of data management tasks needed to integrate biomarker data, safety lab data and any other sources."

Experienced data specialists

With Lab FSPx, clients can better manage laboratory data acquisition, data transfer, data transformation, data reconciliation and site interactions.

By combining Lab FSPx with a client's central laboratory data team, sponsors are often able to complete study start-ups faster by implementing standards, lean processes and blended roles. In fact, an increasing number of sponsors are turning to the FSPx solution as they seek to reduce costs and data reconciliation processes.

When Covance is the central laboratory, sponsors can add to the Lab FSPx service by incorporating streamlined processes for data reconciliation that eliminate bottlenecks and directly access the necessary data stores. Because Lab FSPx also has access to eCRF records, the result is improved start-up, smoother data management during trials and faster data reconciliation.

In leveraging experienced data specialists and clinical programmers, clinical teams can effectively manage studies with a range of laboratories, including central, local and specialty labs via Lab FSPx. This is particularly important in biomarker-rich studies where data is often very complex and there are multiple external labs delivering data.

Essentially, clients gain an end-to-end solution to help them better manage their laboratory data management operations with the Covance Lab FSPx model. Sponsors benefit most from being able to depend on having their data the way they need it, when they need it, via a scalable, outsourced solution.

Medical Device and Diagnostic Solutions: A life cycle development model that moves your device ahead of the game

The medical device and diagnostic (MDD) industry is experiencing a transformational era due to huge advances in technologies such as Artificial Intelligence (AI), robotics, mobile apps, combination products and patient-enabled diagnostic tests.

While these advancements are exciting, they can also bring with them a fresh set of challenges for medical device companies.

A stringent regulatory environment (such as Europe's MDR and IVDR), more complex trials with longer development timelines, as well as reimbursement constraints, are all hurdles in bringing new device products to market.

In response, new approaches to device development are emerging to streamline the process, with the goal to make it easier and more effective overall. One novel model is to integrate the four key components of development that span the medical product's life cycle: preclinical, clinical, regulatory and post-market stages. This integrated approach is helping to simplify product development which, when done with a single research partner, can become even simpler.

Covance works with medical device and diagnostic firms to build a strategic and regulatory-driven plan that addresses development goals across the full product life cycle.

This specialized and flexible approach enables MDD manufacturers to manage their overall development portfolio holistically – from biocompatibility testing and conducting clinical trials, to regulatory submissions and post-market surveillance.

According to Covance Vice President and Head of Medical Device and Diagnostic Solutions Suzanne Carroll: "To answer our clients' innovation challenges, we brought together a cohesive solution for medical device and diagnostic development – one that integrates deep expertise in the medical device and diagnostic regulatory and development space, via a series of strategic acquisitions – combined with Covance and LabCorp core competencies in development and diagnostics," says Carroll.

"With new regulatory requirements and existing guidelines changing, this transforming landscape can make it complex for device companies to efficiently move forward."

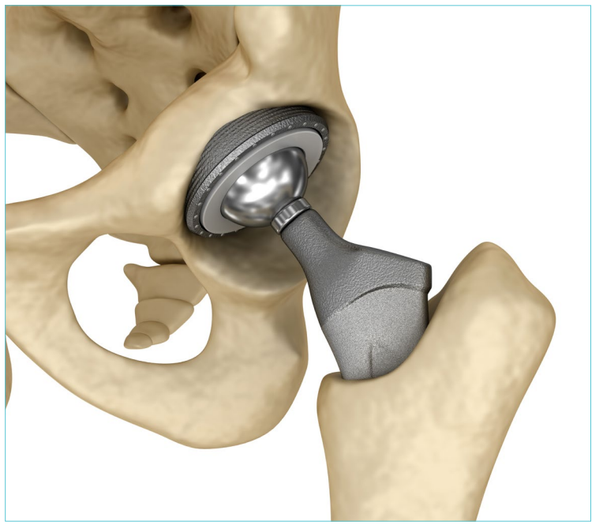
Our recent Medical Device and Diagnostic acquisitions activity includes Chiltern (including the device-focused business of Theorem), PMI (nonclinical device and surgical solutions), Regulatory and Clinical Research Institute or RCRI (a clinical/regulatory team dedicated to medical device and diagnostic development) and assets from ENVIGO (nonclinical and biocompatibility testing).

"The team assembled is deeply experienced and has conducted medical device trials since 1985," explains Carroll. In fact, the Covance team has conducted more than 500 Medical Device and Diagnostic studies, reaching an estimated 110,000 patients in the past five years alone. This extensive experience and commitment to the industry helps clients stay on top of the ever-evolving medical device regulatory landscape while also streamlining timelines and mitigating product development risks.

A medical device and diagnostic powerhouse

"Today, Covance clients have access to a dedicated team and specialized portfolio of solutions that addresses the complete life cycle of medical device and diagnostic products," says Carroll. Furthermore, she sees having the MDD unit within the larger organizations of LabCorp and Covance as a distinct advantage for MDD clients: "As a diagnostic testing and trials business, medical device and diagnostic development fits naturally within our DNA to deliver unique solutions. This is especially true as the lines between device, diagnostic testing and drugs continue to blur."

For example, the combination of the vast number of patient encounters of LabCorp along with Covance's end-to-end contract R&D expertise enables a powerful difference in trial recruitment for the medical device industry. Unique options such as LabCorp's Patient Service Center network, virtual and mobile health capabilities and proprietary data sources are also helping MDD manufacturers gain access to the right patients and uncover patient preferences that better inform clinical study designs to drive stronger recruitment than the industry norm.



Looking to the future

"With new regulatory requirements and existing guidelines changing, this transforming landscape can make it complex for device companies to efficiently move forward. Covance aims to simplify all that," says Carroll. "By combining scientific insight, regulatory guidance and program management, we can work with device and diagnostic manufacturers to help fully optimize development across all stages of their product's life cycle."

The future looks exciting for Covance Medical Device and Diagnostic Solutions clients – gaining a customized model that integrates their plans and improves the overall development process to help bring their products to market faster.

Deciphering real-world data to accelerate clinical trials

As clinical studies get more complex and pressures to deliver increase, trial sponsors are seeking more efficient ways to execute studies.

The use of data to drive smarter decision-making is an important way of supporting a study's end goals. But with so much talk in the industry surrounding data, deciphering what matters is essential.

When it comes to clinical trials, combining de-identified clinical lab results and investigator performance with other routine information can provide significant insights. By linking these datasets, it is possible to conduct research at a speed and scale that outperforms industry norms.

According to Covance Data and Technology Organization Executive Director Dan Ballard, "Data can support a trial's end goals by facilitating more efficient and effective selection of sites and the identification of patients who meet the criteria for the clinical trial."

"Covance has a line of sight to over 50% of all the clinical trials in the world. LabCorp, our parent company, is one of the single largest sources of patient lab data in the world, covering about half the population of the United States. Because LabCorp is uniquely positioned to de-identify lab tests in a HIPAA compliant manner, Covance has access to these de-identified test results and any available corresponding diagnoses codes. The combination of this data makes for very powerful insights related to patient recruitment," explains Ballard.

"We are the only organization in the industry that has this vast volume and powerful combination of data to help our clients design more efficient trials and accelerate their trial recruitment," continues Ballard.

In addition to data on sites and potential participants, Covance also offers voice-of-patient information from its extensive Patient Intelligence Database which provides insights regarding patient tolerances to participate in clinical trials. The data spans 20 indications and is accumulated from 30 different countries.

Voice-of patient-data helps to develop protocol designs that improve patient recruitment and retention by considering patients' needs to make a study more convenient for those living with a disease. For example, this data is used to understand the upper limits of parameters such as number or length of office visits. The data can also be used to fine-tune site selection by understanding how far patients are willing to travel to an investigator site.

It is this combination of datasets that provides Covance clients with unique insights and strong, viable protocol designs for studies with faster patient enrollment, more patients per site and fewer non-performing sites.

"When we identify sites, we're focused on producing a country-wide distribution that will efficiently meet timelines," says Ballard. "If you're trying to beat the timelines, a sponsor could simply add more sites. But then you're doing it faster with twice the number of sites and it's not cost effective."

Beating historical industry performances

Unlike other contact research organizations (CROs) that use prescription data or ICD diagnosis codes, Covance can go another step farther because it is able to analyze de-identified segments of 30 billion test results from approximately 150 million patients for its clients. This significant dataset enables the company to identify clusters of people who likely match a sponsor's trial eligibility criteria while accurately evaluating the impact inclusion/exclusion criteria will have on the overall pool size.

"One reason that clients select Covance is because we generate more clinical trial data than any other company in the world," Ballard explains. "Our analytical expertise enables Covance to turn this into high-value insights surrounding investigator performance across a number of key patient recruitment milestones and metrics to set our client's trial up for success."

"For example, there was a sponsor who awarded their trial on metastatic breast cancer to another CRO. A year into the trial, they came to us because the trial needed to be rescued. We changed the sites chosen which, according to our data, were not the highest performing sites for that particular indication, and put the trial back on track."

"By taking advantage of our large datasets, we were able to add more productive sites to this client's mix and get their recruitment on schedule quickly," states Ballard.

Another client was facing challenges in randomizing 2,700 patients within a narrow timeframe for a suite of registration studies while getting international sites up and running. Covance leveraged its historical investigator database to identify and secure the highest performing investigators and their current site capacity in the indication.

Extensive feasibility outreach and site capacity assessments meant that efficiencies could be identified, enabling effective overlapping of sites across the program and resulting in an accelerated site start-up and reduced clinical costs.

The client achieved its first patient in (FPI) requirement ahead of schedule for all studies in the program, beating the historical industry performance across a number of key metrics, including 18% fewer weeks from final protocol to FPI and 75% more high-performing sites.

Gain an unrivaled combination of data and actionable insights

By leveraging data and understanding where to find potential participants, it is possible for clients to accelerate a trial by applying critical insights across multiple therapeutic areas and indications. This leads to improved protocol designs, better patient recruitment and retention and ultimately, getting medicine to patients faster.

Clients that take advantage of the Covance-exclusive industry data can more accurately identify high-performing investigators and clusters of eligible patients to benefit a trial. They are also able to realize lower study costs, reduce time-to-market, and improve forecast accuracy.

What's more, with the continued growth of datasets and ongoing developments in genetic data, it seems the potential to accelerate clinical trials has only just begun.

▶ By leveraging data and understanding where to find potential participants, it is possible for clients to accelerate a trial by applying critical insights across multiple therapeutic areas and indications.

Biosimilars: The next chapter for biologics begins

Biosimilars – biologic drugs with a high degree of similarity to previously-approved innovator biologics, hit full steam in 2019, with the development pipeline exceeding predictions of industry analysts.

This trend shows no sign of slowing down, with the global biosimilars market expected to grow to more than $15 billion by 2024.

So why the sudden spike in interest? As more biologic innovators are set to lose patent protection within the next five to 10 years on their biologics, this opens the door for biosimilar developers to move into the market.

Another driver is the biosimilar approval pathway cost benefit which, according to the U.S. FDA, is based on demonstrating biosimilarity or interchangeability with the innovator's approved reference product rather than independently demonstrating the safety and effectiveness of the biosimilar[1].

While proving biosimilarity requires rigorous analytical testing early in the development pipeline, organizations could save on the financial outlays with biosimilars since the approval pathway has different requirements. For example, the expense of developing a biosimilar is radically less than developing a product from the ground up, costing between $75 and $250 million[2] for the former, versus around $2.6 billion[3] for an innovator.

Sian Estdale, Global Scientific Head, explains: "Biosimilar developers are following the model of generics. When the patent expires, they have the opportunity to create their own generic molecule that may be interchangeable with the referenced innovator product at lower development costs. However, this is easier to do for organic synthesis of a small molecule than for biologics."

"Because of that, the anticipated price savings between the biosimilar and the reference product aren't as substantial for biosimilars as they are for generics, but the savings have been better than originally anticipated."

"Initial estimates were that biosimilars would be about 80% of the market price of the reference product[4], but we have seen sale price levels that are much lower for certain products. This is helping to make biosimilars more accessible."

The scrutiny over drug prices could boost the adoption of biosimilars since the cost estimates are much less than innovator therapies. The reduced approval timelines involved are also likely to tempt companies to explore this market.

"The historical innovator process took between 10 and 15 years to achieve marketing authorizations," explains Estdale. "However, with new gene therapies we are seeing very rapid development timelines."

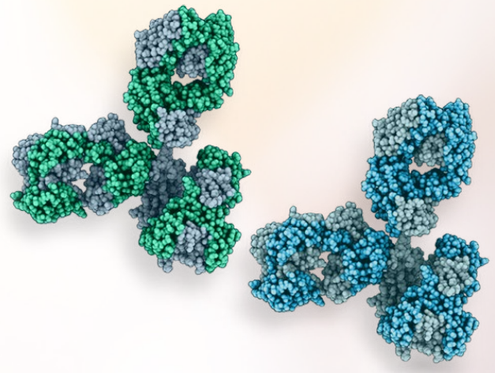
This sped-up process is largely due to the nature of the patient groups and the support of regulators, with some organizations reaching completion at the four to six-year mark.

"Initial estimates were that biosimilars would be about 80% of the market price of the reference product, but we have seen sale price levels that are much lower for certain products."

However, when it comes to the patient recruitment process for biosimilars, organizations are facing fresh challenges. Because biosimilars are not a novel treatment, but rather a treatment paradigm that has been in use for some time, garnering patient interest can be difficult. For most patients, novel treatments are preferred, especially if they have found little success with the existing treatments available.

One alternative is to execute studies for biosimilars where easy access to the innovative product may not currently exist.

According to Alicia Baker, Head of Biosimilars: "There are numerous clinical studies being sited in eastern Europe and Latin America, where the healthcare systems may not reimburse or pay for expensive existing biologic treatments. We find patients in these areas are more interested in participating in biosimilar trials, due to less access to this type of treatment."



Biosimilars – biologic drugs with a high degree of similarity to previously-approved innovator biologics,

Achieving a description of biosimilarity

Gaining an understanding of what is important for a particular molecule alongside the knowledge of what regulators are looking for helps sponsors build a successful description of biosimilarity. For organizations exploring biosimilars, the full-service regulatory department at Covance can help by developing a strategy, engaging in a dialogue with agencies and other stakeholders and executing a plan in terms of submissions and publishing.

To help expedite biosimilar development, Covance created a series of Analytical Master Files for biosimilar testing. “These were produced to answer clients’ common questions and efficiently consolidate our methods of development for the same molecules,” explains Estdale.

“Clients are excited to learn that we are extremely familiar with biosimilar pathways and the regulatory expectations, and they gain additional value having answers to the key biosimilar questions upfront, making the process even more efficient.”

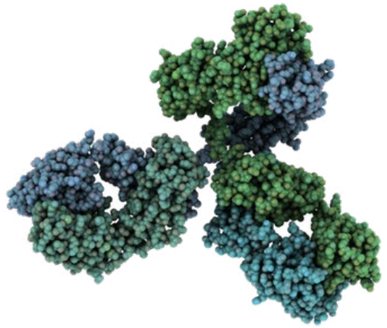
Pre-designed solutions from Covance have the power to save biosimilar developers between six and 12 months. “By conducting rapid development ahead of time that validates fit for purpose and appropriateness for characterization, clients can describe initial milestones for their innovator criteria and biosimilarity,” says Estdale.

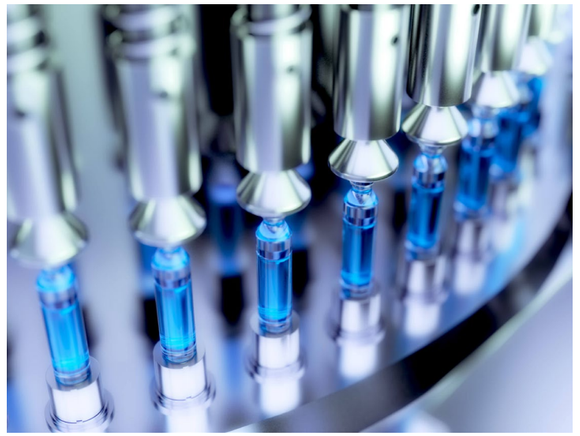
The future of biosimilars

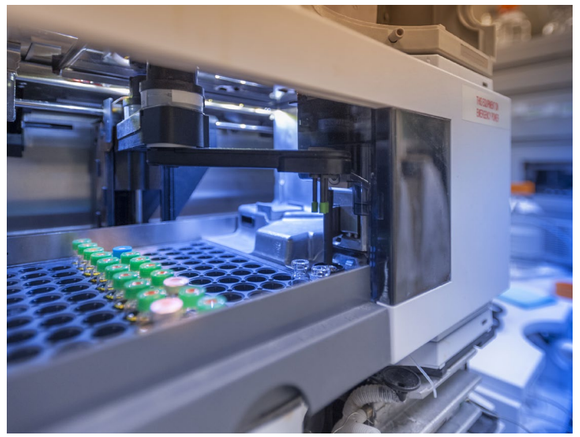
While there has previously been some uncertainty around the uptake of biosimilars, the industry is seeing a sharp increase in activity, with Europe already well established in the arena.

Given the relatively recent introduction of specific guidance by regulatory authorities, the process remains in its early days, but the industry is gradually becoming more familiar with processes and approval pathways, which is fostering an improved environment of approval for biosimilars.

With a greater probability of success via earlier biosimilarity assessment and projections suggesting up to a 30% value on market[5], it’s clear that the next chapter for biologics is one to watch.







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