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RELEASING THE BRAKES:
How New RTSM/IRT Solutions Will Accelerate Drug Development

IN PARTNERSHIP WITH

ORACLE®
Health Sciences

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FOREWORD

> As Oracle continues to advance solutions for clinical development, we wanted to understand more precisely where the specific pain points exist for our customers.

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PHARMACEUTICAL COMPANIES TODAY invest billions of dollars in the development of a single innovative new medicine. That investment, along with the competitive nature of the business and the urgency to deliver treatments for patients in need, puts companies under enormous pressure to reduce the time it takes to bring a new drug to market.

In turn, this puts a great deal of focus on the evolving clinical trial process and the technology that supports it. Pharma companies are demanding that clinical operations teams move much faster, despite the fact that trials have become more numerous and more complex than ever.

For example, telemedicine has made the development of the "site-less" clinical trial possible, where the trial goes to the patient instead of the patient going to the trial, and where wearable sensors play a big role in providing far more data about those remote patients than ever before. Medicines based on immunotherapy, genomics and other scientific advances are changing the nature of trials even further, but also make it more challenging to identify, recruit and maintain the proper patient cohorts. And on top of this, regulators around the world continue to issue new guidelines for clinical trials design, conduct, and reporting that must be incorporated into the process.

While technology vendors have stepped up to support the needs of the various teams involved in clinical development to improve efficiency over the past 20 years, this innovation has taken place in functional silos. The result is a collection of point solutions that don't "talk to each other" and now actually contribute to overall process inefficiency with redundancy and manual effort slowing things down. One area particularly affected by this fractured environment is drug randomization and supply management.

As Oracle continues to advance solutions for clinical development, we wanted to understand more precisely where the specific pain points exist for our customers. We worked with Pharma Intelligence to survey professionals in the field and learn more about their needs, specifically around randomization and supply management.

First and foremost, clinical study teams told us they are frustrated with the lack of integration between their Randomization and Trial Supply Management (RTSM) systems and other clinical platforms. They're also concerned about the lack of flexibility their systems have when it comes to implementing mid-study changes – and almost everyone we surveyed told us they typically deal with one or more such study changes that slow the process by weeks. Understanding these frustrations is the first step in meeting the needs of the industry in the future.

Our goal in conducting this research was to ensure we are addressing the top challenges of our customers and delivering what the market wants in a modern RTSM solution. That's not only good for our customers it's great for the ultimate beneficiaries of clinical trials: Patients. The more we can help clinical trials move faster in a safe and effective manner, the more we accelerate the pace of new medicine and as millions of patients wait with hope for the next innovation.

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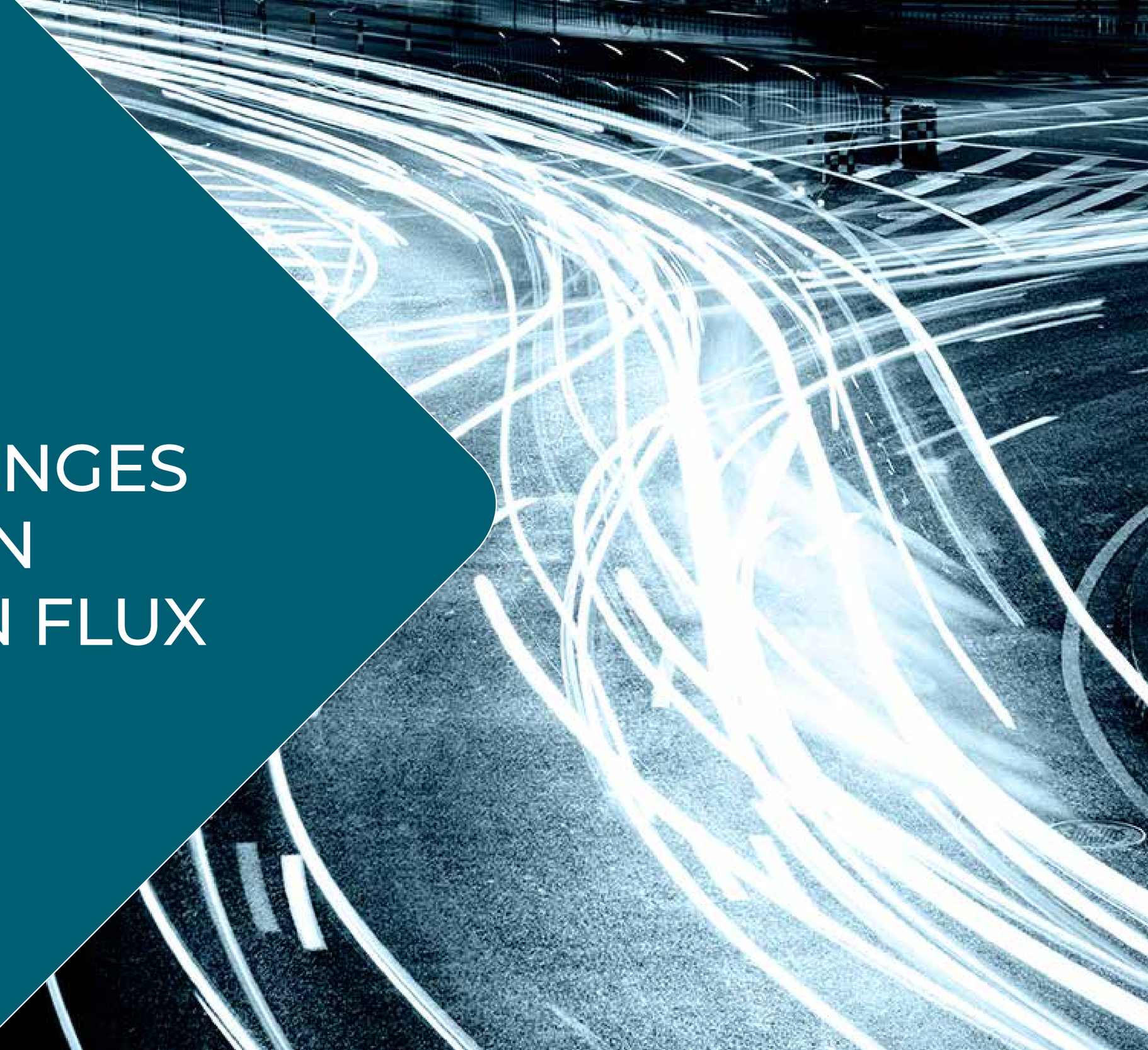
THE CHALLENGES FACED BY AN INDUSTRY IN FLUX



POWERFUL FORCES ARE RESHAPING CLINICAL TRIALS. Faced with the urgency to advance new therapies to meet the needs of patients, beset by generic competition and pricing pressures, sponsors are running complex studies designed to differentiate their innovative drug candidates from the pack. In theory, these trials should be getting faster and more efficient due to the availability of more data and technology. Yet, the ubiquity of silo'ed eClinical systems that don't easily connect to each other means this theory is yet to translate into practice.

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The struggle to leverage technology that truly meets the needs of today's trials underpins some of the industry's problems. At a time when other sectors are reaping the productivity-boosting benefits of technology, the pharmaceutical industry is seeing the inflation-adjusted cost of drug development double every nine years[1], which neutralizes the positive impact of process improvement. With clinical trials accounting for two-thirds of the cost and duration of R&D,[2] it is clear where a big part of the problem lies. It's not that the technology to support clinical trials doesn't exist; the issue lies in the lack of advancement of that technology to meet the needs of today's clinical trials. Legacy clinical trial technologies were created as point solutions to manage specific parts of the trial process independently, which at the time was a big improvement over manual processes, but didn't have the big picture in mind. Over time, organizations tried to stitch these point solutions together to create a more connected process, but as a result they actually created new barriers to achieving efficiency and speed.

One point solution developed with the goal to improve efficiency was Randomization and Trial Supply Management (RTSM), also

referred to at times as Interactive Response Technology (IRT). And while RTSM/IRT solutions have saved companies time and resources by automating the randomization of patients and supply of study drugs, the current technology isn't meeting the needs of today's clinical trial supply managers and clinical operations teams. It's time for technology to catch up to the critical needs of the industry.

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WHY A NEW APPROACH TO RTSM/IRT IS NEEDED

THE SHORTCOMINGS OF RTSM/IRT SOLUTIONS STEM FROM the pace of change in the clinical trial sector, which is designing and running increasingly complex studies that require highly-flexible technologies. These changes have created a disconnect between what study teams need and what RTSM/IRT solutions can provide.

This disconnect is evident in results from a recent survey of professionals in clinical operations, trial supply management and related functional areas. The survey conducted by Pharma Intelligence and Oracle Health Sciences sought to understand the frustrations clinical teams have with existing RTSM/IRT systems, and what they want and need from this technology to make their job easier.

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Integration emerged as the biggest issue, with 74% of respondents saying it is challenging to connect their RTSM/IRT systems to other eClinical platforms. Sponsors want the vast array of technologies now needed to design and run clinical trials to connect to each other easily and seamlessly, removing the redundancies and manual effort currently required to manage a trial. While, vendors have tried to integrate these siloed systems, the survey suggests these efforts have failed to fully address the problems.

Respondents also zeroed in on shortcomings of RTSM/IRT solutions themselves. Many of these issues are interrelated. For example, 71% of people cited a lack of flexibility and inability to support study changes as a top pain point. This frustration is tied to the fact that today's systems are not self-service, and sponsors need to ask the

RTSM/IRT vendor to make the changes. With 92% of clinical teams needing to update their IRT systems due to minor trial amendments such as new inclusion criteria, the reliance on vendors ties their hands and delays their studies.

The reliance on vendors creates other issues, too. Most respondents cited the review and validation process, the time needed to build, test and deploy technologies, and reliance on vendors to perform these tasks as significant challenges with their existing RTSM/IRT solutions.

These problems have real impacts. The survey results suggest it typically takes 6.5 weeks to build, deploy and validate an RTSM/IRT solution, with some respondents indicating that they have waited more than 10 weeks for a vendor to complete these tasks. These prolonged timelines have multiple detrimental effects, from delays to the start of clinical trials to a reduction in overall clinical trial activity.

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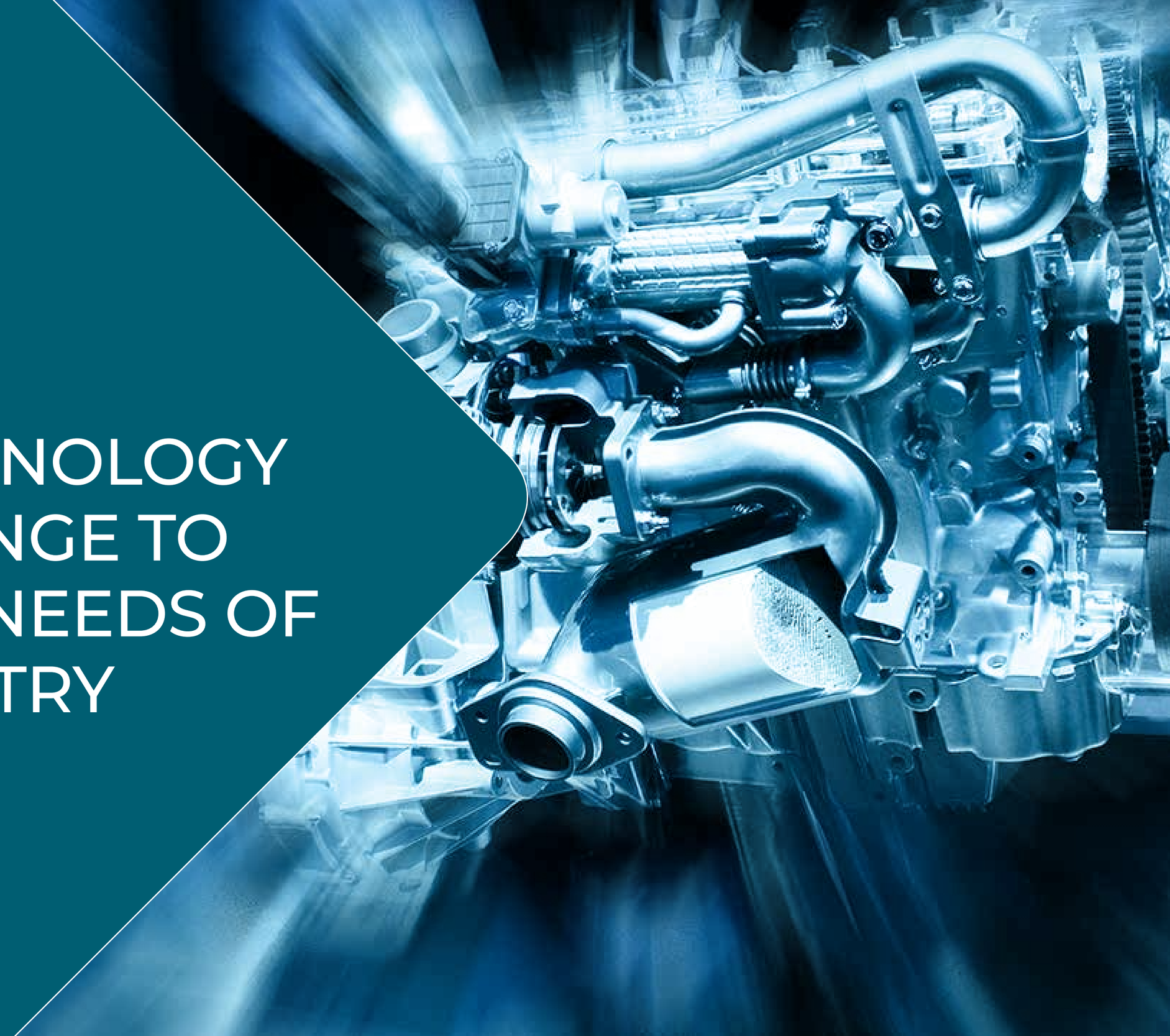
HOW TECHNOLOGY MUST CHANGE TO MEET THE NEEDS OF THE INDUSTRY



TECHNOLOGY SHOULDN'T CREATE PROBLEMS; IT SHOULD SOLVE THEM.

RTSM/IRT technology solved some significant problems when it was first introduced in the 1990s. It represented a great advance for the industry, streamlining what, until then, had been a highly manual process, by automating it and moving it online. These new RTSM platforms reduced paperwork and cut the time required to set up and implement a study. However, these platforms were developed as independent point solutions at a time when there were far fewer demands on the clinical trial process, and far fewer trials overall.

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Fundamental to our approach is providing capabilities rather than systems.

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Today, research-based pharma companies have close to 15,000 products in their pipelines; and, the nature of the products and the supporting clinical trials are likewise more complex. That's led to the problems identified in the survey -- problems that legacy RTSM platforms can't address.

The finding of the research suggest the industry needs a fresh, new approach to how technology supports clinical trials – not tied to the limitations of the past, and considering the technology innovation available today and in the future. As the leading eClinical provider in the market, backed by the development teams of the second-largest software company in the world, Oracle is well-positioned to answer this call. Oracle Health Sciences is leading the way in "next generation" clinical trial technology with the recent launch of its new Clinical One Platform. With Clinical One, Oracle Health Sciences has reimagined the way technology and information are used in clinical research. It provides universal access to information that only has to be captured once and common tools that can be used across all processes.

Fundamental to our approach is providing capabilities rather than systems. This allows things to be broken down into smaller modules that remove the complexity required by a systems approach. By unifying those capabilities into a single platform, Clinical One eliminates the interoperability and integration problems that affect legacy RTSM technology.

The RTSM function is critical to getting a trial up and running, so with that in mind, Oracle developed the randomization and supplies management module of the Clinical One platform first (Oracle Health Sciences Clinical One™ Randomization and Supplies Management Cloud Service). In the near future, the electronic data capture module

will be layered on to the RTSM foundation already built in Clinical One. Knowing that the industry can't make the switch to a highly innovative solution like Clinical One overnight, Oracle has ensured that this new technology can integrate not only with legacy RTSM systems, but with other legacy clinical trial solutions as well, including EDC and CTMS systems to name a few. This way organizations can transition to a modern eClinical environment, smoothly and at their own pace. This approach is enabled with cloud technology supporting a single

> Study teams can manage studies themselves in real-time through the 100% self-service platform and intuitive user interface of Clinical One.

data model for Clinical One. Data is entered once and then made available to all the other modules and their users, as needed, at every step in the clinical trial process. This makes it possible to create a study in which patient data capture and management, study design, site management, screening, inclusion/exclusion criteria, protocol deviation, adverse event reporting management and more are shared across all functional areas and teams involved in a study. Clinical One Randomization and Supplies Management Cloud Service is a versatile solution. Study teams can manage studies themselves in real-time through the 100% self-service platform and intuitive user interface of Clinical One – from initial study design and start-up, to mid-study changes – or; they can leverage the vast experience of Oracle's team to assist with the design, build and deployment of their studies. Having these options enables organizations to focus on their expertise and get studies up and running as quickly as possible.

With Clinical One, it has become possible to reduce the study start up times from weeks to days, and to support mid-study changes

without causing disruption of the trial. It also makes possible a future where clinical trials are conceived and implemented in new ways – for example, by randomizing a patient even before they see a clinician, or allowing patients to "see" investigators remotely and shipping drugs directly to the patient, supporting the advent of the "site-less" trial.

Clinical One represents a significant re-imagining of clinical trial technology, not only RTSM, but the entire clinical trial process. This new approach will restore the promise of technology to speed clinical trials—not slow them—which will help get new therapies to market faster for patients in need.

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HOW RTSM/IRT CAN ACCELERATE R&D

A BETTER, FASTER APPROACH TO RTSM/IRT WOULD LEAD to significant improvements in clinical trials. If a drug goes through five clinical trials on its path to market, a sponsor could spend one year working with vendors to build, deploy and validate RTSM/IRT solutions. Even if each deployment was faster than is typical today, the sponsor could still spend more than six months on RTSM/IRT tasks for a single drug.

That creates an opportunity for RTSM/IRT solutions that are quicker to set up to have a real impact on clinical trial timelines. Self-service RTSM/IRT systems are expected to cut setup times from weeks to days. Scaled across a clinical development program, such time savings would result in therapies getting to market many months, perhaps even a year, sooner. These savings benefit patients and the finances of drug developers.

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Sponsors that adopt next-generation RTSM/IRT systems stand to control R&D spending while accelerating and expanding development, enabling them to get more life-changing medicines to market.

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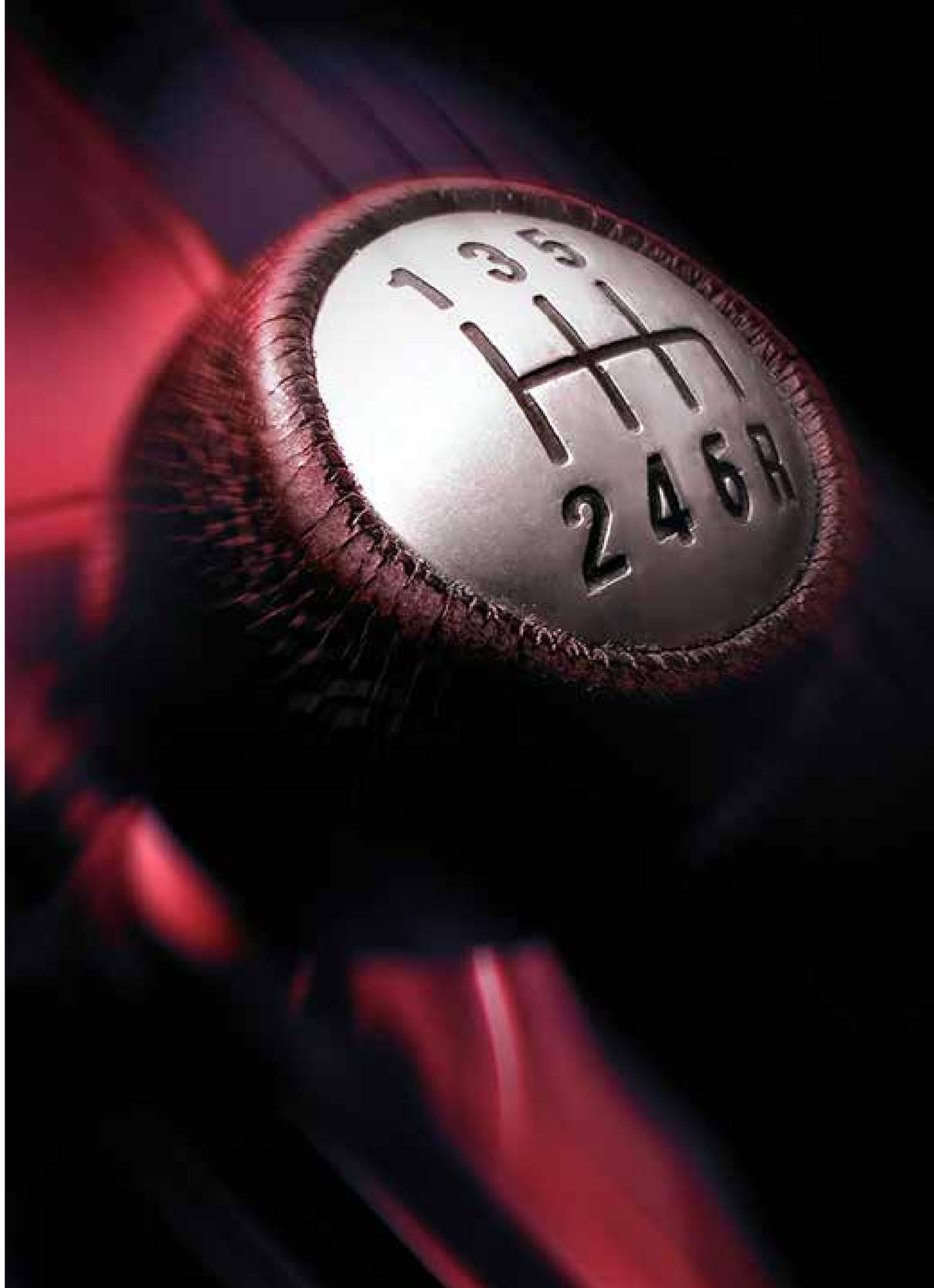
Following the ripple-out effects of these efficiency gains shows the benefits could be even more far reaching than anticipated from a preliminary analysis. Notably, two-thirds of survey respondents said cutting RTSM/IRT timelines from weeks to days may enable them to run more clinical trials. In this way, new RTSM/IRT systems will do more than accelerate drug development. They will expand its frontiers.



Empowered by self-service RTSM/IRT systems, sponsors may have the resources to run more clinical trials. One sponsor could run a somewhat-speculative trial in a different indication, creating a chance to address an unmet need and open up a new market for a therapeutic. Another sponsor may allow more assets to advance into human testing, minimizing the risk that resource prioritization will cause effective drugs to languish in its preclinical portfolio.

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This app-enabled approach has multiple upsides. Site staff equipped with RTSM/IRT mobile apps will enter data into the system faster, cutting the risk that administrative backlogs.

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All these gains stem from one improvement to RTSM/IRT systems, namely the shortening of setup times. Other improvements will unlock additional gains. Making RTSM/IRT systems part of larger eClinical platforms is expected to simplify integration — resolving the biggest pain point identified by survey respondents — while eliminating data duplication and allowing for one-time entry of data across sites. These improvements will free sponsors to focus time and resources on drug development instead of low-value process and admin work.

The rise of mobile technology will lead to additional benefits. Today, it's typical for staff at a clinical trial site to manually update RTSM/IRT systems when study drugs arrive, are dispensed or are returned. Mobile apps could automate these data entry tasks. All the information about a medication kit is held in its barcode. Scanning the barcode with a camera on a mobile device could allow site staff to pull up all of this information and update the status of the associated medication kit in the RTSM/IRT system.

This app-enabled approach has multiple upsides. Site staff equipped with RTSM/IRT mobile apps will enter data into the system faster, cutting the risk that administrative backlogs will negatively impact the operational efficiency of the study center, and by extension, the progress of the trial. The automation of data entry will also dramatically cut the likelihood of errors, that inevitably occur with manual human effort, that could lead to participants receiving the wrong study medication.

The currently available RTSM/IRT systems make it possible for medication errors to happen. One study found the average annual error rate in a clinical trial was 0.35%.[3] With the United States Food and Drug Administration calculating that more than 100,000 people participated in pivotal clinical trials alone in 2015,[4] cutting the error rate could stop hundreds of patients from receiving inappropriate and potentially dangerous doses every year.

SUMMARY

In these ways, next-generation RTSM/IRT solutions stand to pull off the rare feat of making a system both faster and safer. Having made do with solutions that lagged behind their needs for years, sponsors can now look forward to using RTSM/IRT systems that keep pace with their requirements and thereby eliminate many of the challenges they have faced in recent years.

These systems will feature the simple plug-and-play connectivity sponsors want, ending the long wait for interoperable eClinical technologies. The systems will also be more flexible and give back control to the trial teams. Instead of having to wait for vendors to set up the system and make mid-study amendments, sponsors will be empowered to make the changes themselves. Many of the pain points identified by the surveyed clinical trial professionals will fade away once these RTSM/IRT solutions are adopted.

The scale of the broader challenges faced by the industry means these improvements cannot come soon enough. Sponsors that adopt next-generation RTSM/IRT systems stand to control R&D spending while accelerating and expanding development, enabling them to get more life-changing medicines to market.

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