Veeva

# A Digital Future: Evolving Beyond Decentralized Trials

## Introduction

The acceleration of digital transformation, in the wake of COVID-19, has had a significant impact on the industry. New technologies and tools enable decentralized clinical trials that help speed execution for specific processes. Yet, the addition of multiple function-specific eClinical applications to an already complex systems landscape makes it more difficult to run trials efficiently.

Nearly all sponsors and CROs report significant challenges with decentralized trials, including site technology adoption and increased burden for technology-averse patients. Only 56% say that the shift to decentralization has improved the patient experience, and less than a third say they have seen improvements in site engagement.

Pharmaceutical companies, biotechs, and CROs are rethinking their trial strategies and moving beyond decentralization for a more connected and digital trial model. The outlook is bright for clinical trials, and several companies–like AbbVie, Bayer, Celerion, GSK, Labcorp, and LEO Pharma–are helping to pave the path to the future.

The following eBook provides insights into the key challenges of decentralized trials, how the industry can advance toward a digital and connected future, and the critical need for a strong data foundation. It also showcases a top 20 pharma, Bayer, and how they are taking steps to enable digital execution for seamless data exchange in trials.

ARTICLE 1

## Overcoming Growing Pains with Decentralized Trials

Success with patient-centered digital clinical trials hinges on engaging patients in various ways and managing huge volumes—and new forms—of data. This article explains the challenges and shortcomings of decentralized trials, and why companies need to look beyond decentralized study models to enable a digital and connected trial ecosystem.

READ IT HERE ▶

ARTICLE 2

## Clinical Trials Prepare for a Digital, Connected Future

The shift to hybrid, decentralized trials has highlighted the need for better data management and direct digital connections that link sponsors, sites, and patients. This article discusses why trials must become wholly digital from start to finish, supported by optimized technology for site and patient convenience.

READ IT HERE ▶

ARTICLE 3

## Data First: Building a Foundation for Digital and Decentralized Clinical Trials

Without a strategy for managing clinical data centrally, sponsors lack the visibility needed to optimize trial outcomes. Lack of complete and concurrent data can compromise patient safety and backtrack progress toward more agile and adaptive trials. This article covers the critical role of data management and why a modern infrastructure is key to digital trials.

READ IT HERE ▶

ARTICLE 4

## Clinical *Kaizen* at Bayer: Moving Past Spreadsheets to Unify Operations

Bayer addresses the use of manual processes and spreadsheets to conduct trials. This article showcases how the company drives continuous improvement by leveraging unified applications to enable a digital and connected clinical ecosystem.

READ IT HERE ▶

ARTICLE 1

# Overcoming Growing Pains with Decentralized Trials

**By Jim Reilly, Vice President of Vault R&D and Quality at Veeva Systems**

Decentralized clinical trials (DCTs) have been around, in some form, for over a decade. At the time, industry leaders praised the concept behind DCTs and the drive to make trials more convenient for patients, but many companies found the model too complex for mainstream use.

Then along came the COVID-19 pandemic, which opened the door for disruptive change, as Mayank Anand, vice president, global head, data strategy and management at GSK, told attendees at the Veeva R&D and Quality Summit.[1] As restrictions forced companies to adopt new tools and workflows to keep their pipelines alive, the deficiencies of traditional clinical trial approaches became clear. So, too, did the technology fragmentation that had resulted from quick implementation of stand-alone digital tools.

Today, sponsors and CROs are considering how to optimize clinical trials for the future. Although the industry speaks of DCTs, the need for patient-centricity is likely to dictate hybrid approaches that combine decentralized and site-based functions and maintain some human interactions within a digital framework. **Figure 1** outlines distinctions between some of the various terms now being used to describe modern clinical trials.

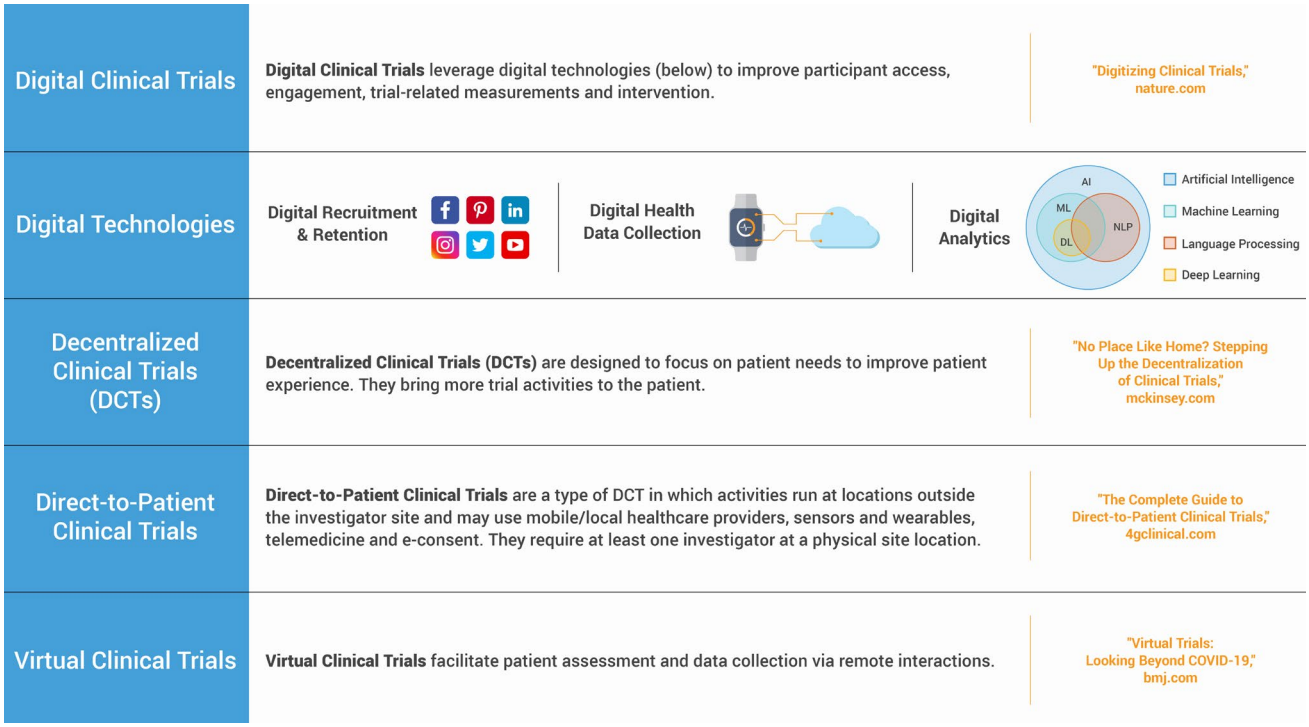
## Data Now at the Center of Everything

As the industry moves toward that goal, companies are refining digital strategies, making trial designs more patient-friendly, and connecting more closely with clinical research sites. Some are also strengthening the foundation for digital trials by automating data aggregation, harmonization, and cleaning, all of which are crucial to future success, as growing volumes of diverse data flow into trial databases from wearables, sensors, and continuous monitoring devices.

“Data management was once an invisible function, but it is now at the center of everything. Data has become the new currency,” said Anand, who described the company’s collaboration with Veeva on Veeva CDB, a clinical database that will aggregate and align data from sources outside of the EDC for centralized cleaning and reconciliation.

[1] Veeva Systems, Veeva R&D and Quality Summit Connect, 2021

FIGURE 1: DIFFERENT ROUTES TO PATIENT CENTRICITY




Source: Veeva Systems

## Unfulfilled Promise, Rising Expectations

Results from Veeva's Digital Clinical Trials Survey reflect the progress that sponsors and CROs are making with clinical trial modernization, the challenges they still face, and the growing pains that accompany any major technology and business shift. Of the more than 280 clinical leaders who responded to the survey, only 27% ran DCTs before the pandemic, but 87% are now working with DCTs or soon plan to, while 95% expect to increase their use of DCTs over the next year.[2]

Although DCTs promise to address patient recruitment challenges and reduce study costs and timelines, their full potential will take time to realize. Less than one third of Veeva's survey respondents have seen DCTs lower costs or shorten trial timeframes.

In addition, only 56% of the sponsors and CROs surveyed said that moving to DCTs has improved the patient experience. In fact, half of them see DCTs as imposing a greater burden on patients, some of whom are not comfortable with digital technologies. Whether truth or fiction, stories are circulating about trials in which older clinical trial patients have asked their children or grandchildren to help them with, or take over, entering data into a smart phone application.

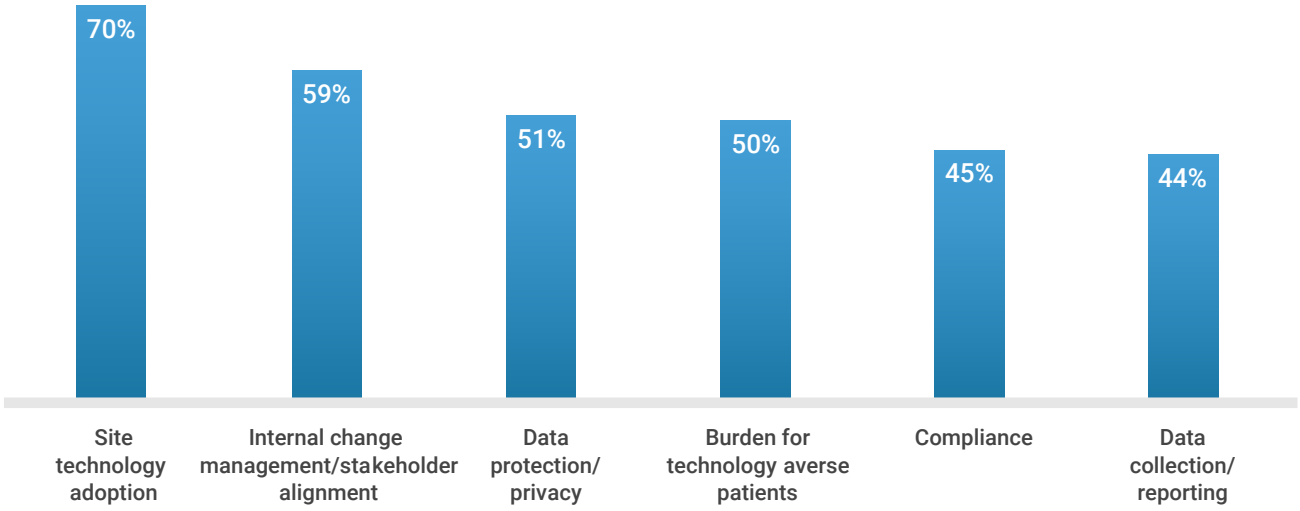
Virtually all respondents —a full 99% —acknowledged the technical and organizational difficulties posed by DCTs (**Figure 2**), with 70% pinpointing research sites' adoption of new technologies as the top challenge. There is a technology disconnect between sponsors and sites, with some sites reporting that staffers spend

[2] Veeva Systems, Veeva Digital Trials Survey Report, 2021

70% of their time on manual processes such as emails. The typical site today uses at least 12 different systems to collect and capture clinical trial data, with sponsors providing customized solutions. The result has been a proliferation of one-off point solutions, and an administrative tangle of logins, access codes, passwords, and portals.

FIGURE 2: BARRIERS TO PATIENT- AND SITE-CENTRIC TRIALS

Nearly all sponsors and CROs (99%) report significant challenges with decentrailzed trials.




Source: Veeva Systems

In addition, 59% of sponsors and CROs saw internal change management as a key challenge with DCTs.

## Companies Taking Action

The industry needs to bring the "back office" of sponsor operations to the "front office" of site- and patient-facing technology. Tackling fundamental problems with patient outreach and data standardization, integration, and management will be crucial. Adopting a platform-based approach would end the fragmentation that has limited collaboration between sites and sponsors, and resolve the data interoperability challenges that patients, sites, and sponsors continue to face. Eliminating paper-based processes by connecting clinical operations, research sites, and patients will cut clinical trial costs and timelines by 25%.

Most survey respondents note that they are actively addressing these obstacles; 66% of CROs and 53% of sponsors reported that they are increasing their support of clinical research sites. CROs led sponsors in adoption of specific measures, with 54% improving data sharing and collaboration (vs. 38% for sponsors), and 54% addressing system interoperability issues caused by the rapid deployment of eClinical technology to support DCTs, compared with 29% of sponsors. On the change-management front, respondents said they are stepping up efforts to update SOPs that were originally written for traditional trials to the new trial environment and reaching out to staff with targeted communication and training.

## Redefining Patient Centricity

Companies will need to look more deeply into what defines patient centricity to determine the best technologies or healthcare approaches to use. “The best choice will differ depending on indication and age group, and the regulatory requirements will determine what can and can’t be done in each country,” says Richard Young, vice president of Vault CDMS at Veeva Systems.

One patient may prefer to have data collected in person at a clinic, another may opt to have it done during a telehealth visit, a third may want to enter it themselves on a smartphone. And all these options could apply to the same patient at different times.

## Retaining the Human Touch

Human touch and interaction are still needed for clinical trials on the patient-facing side and to analyze and optimize data. Using applications to collect data and connect with trial participants delivers patient convenience and execution speed, but it doesn't make up for human-to-human interaction. Studies that include strategies for both digital engagement and in-person patient care can ensure patient centricity and compliance.

The need for patient centricity will also call for data managers and scientists to play a more visible role in early trial design and protocol development. Typically, the easiest type of data to manage has been manually entered site data, where there’s often a binary yes-or-no answer, resulting in a single data point flowing through the system. It’s much more difficult with data that is captured during continuous monitoring, such as with an electrocardiogram, which requires interpretation by an electrophysiologist.

A cross-functional approach involving health care professionals and data scientists will be crucial. The data formats could differ between different systems, even for the same type of data. You may also be capturing the data at different frequencies. For example, if a patient’s heart rate is being measured in the clinic, that will result in a single data point. If the patient is using a heart monitor or a continuous reading via a wearable device, that will result in continuous, high-frequency data. In the end, these data collected at different frequencies must be reconciled and interpreted for results. You may have to contend with and manage huge amounts of data, but it will be critical to determine and focus on, the resultant data.

With patient focus driving the front end, better data management promises to improve overall agility and enable such things as real-time interactive dashboards for data managers, says Anand. GSK’s use of advanced clinical data management systems aims to reduce trial build and lock times by 50-60% and to make agility a cultural goal.

Once key challenges are addressed, modern approaches to clinical trials promise to reduce the time it takes to deliver new therapies.  For oncology drugs, the need is especially urgent. “For some types of cancer, one to two patients are lost every minute. Can the industry continue to do trial locks in 21 weeks instead of four or even two weeks?” Anand asked. “Our patients are waiting,” he emphasized.

**ARTICLE 2**

# Clinical Trials Prepare for a Digital, Connected Future

**By Jim Reilly, Vice President of Vault R&D and Quality at Veeva Systems**

Clinical research has made dramatic advances within the past few years, with new master protocol designs such as umbrella and basket trials emerging. On the operations side, companies forced to adapt to COVID-19 restrictions proved that they could succeed with novel approaches including remote site assessments and decentralized trials. "Before the pandemic, every company had started to dip its toe into the digital world, but COVID-19 pushed us all into the pool. We have had to come up with solutions really quickly to keep our studies afloat, and now it's forcing us to be a little bit more forward-thinking," said Lorena Gomez, senior director, global study start-up, PRO management, and digital implementation at AbbVie.

To improve clinical trial efficiency and quality, the industry must shift to a complete and connected digital trial ecosystem that allows for seamless data exchange and execution. To make this a reality, clinical leaders will need to rethink trial strategies, move beyond decentralization, reduce the technology burden placed on sites and patients, and establish a clinical database foundation.

Many of the early COVID-19 decentralized trials underscored inadequacies. Lingering manual and paper-based processes were found, as well as disconnected e-Clinical solutions at the patient, sponsor, CRO, and research site levels. "It's great to have digital, but now investigators have 10 logins instead of one. It's challenging from a site perspective to be able to execute trial processes through 10 different systems," says Staci McDonald, executive director of scientific clinical operations at the research site network, Celerion.

As the industry considers the next step in clinical operations and data management, the end goals haven't changed. Sponsors still want trials to run as efficiently as possible; patients need easier ways to connect with sponsors and sites; while sites want to simplify operations so they can focus on patients. Only now, the industry must evolve beyond one-size-fits-all thinking about decentralization for a deeper understanding of site- and patient-centricity, and a connected approach that will simplify data sharing and enable seamless execution.

To reap the benefits of decentralization, trials must become wholly digital from start to finish, with technology being optimized for site and patient convenience, to:

- Promote easy, effective patient engagement
- Bring remote capabilities to the research site
- Move to site-focused, -owned, and -controlled systems for site operations
- Extend data cleaning, aggregation, and management from the back end of sponsor systems, to connect better with the front, patient-facing side of clinical operations.

"It's important that we collaborate strategically, as an industry, to understand how decentralized trials will affect the patient journey and site relationship," says Mark Morais, president of clinical operations and commercial solutions at LabCorp Drug Development.

Sponsors and CROs see a need for simplification and standardization, and a greater focus on data. "We have to think about the impact to sites, protocol design, and patients, especially in terms of what we're capturing and how. We must let digital drive simplicity as we potentially increase all the disparate data sources," Morais says.

Decentralized trials will, by definition, require much more data —most of it from wearables and sensors—and that data will need to be ingested, aggregated, and cleaned, says Mayank Anand, vice president, global head, data strategy and management at GSK. "The sharing of data itself is a challenge. Every study brings its own complexity because you have 10 to 15 different external data providers, and everyone uses a different way to inject data. How will we standardize once we go to 20 or 30 different data sources? We need to bring simplicity and a connected architecture," he asks.

To enable this simplicity, sponsors, CROs, and sites will start to take a unified digital approach to clinical trial data and documentation—one that standardizes processes and speeds access to relevant data, whether for study planning and setup, site activation, monitoring and management, document and data management, or study closeout.

## Vital Role for Research Sites

Even though aspects of each trial can be decentralized, sites will continue to play a vital role as a touchpoint for patients. Today, more sponsors support site-centric solutions, moving the industry closer to a model in which sponsors, sites, and patients are connected for seamless study execution and data flow.

Digitizing information will improve its flow. We estimate that it can reduce trial costs and timelines by 25% and lead to more effective communication and data and document sharing in a decentralized trial environment. This strategy demands a deeper understanding of patient and site preferences and needs, with a more robust data standardization and management approach.

## Patient Convenience

Recently, sponsors have focused on patient convenience as the key to engaging and retaining patients. Results of Veeva's survey suggest that sponsors see data security and patient education as keys to improving decentralized trials (**Figure 3**). Improving patients' data security and confidence in that security and developing better ways to educate and inform patients during and after each trial, will be required.

Eliminating the technology burden for patients is another priority. In exchange for reducing the need for travel to sites, the first generation of remote COVID-19-era trials often weighed patients down with numerous digital applications, each designed for one specific function (e.g., registration, site communication, or dosage compliance). Sponsors and CROs recognize the need to address this problem.

Experience with recent decentralized trials also suggests that approaches to patient engagement will need to be varied and personalized. The 19-year-old participating in a new acne treatment trial and the 80-year-old cancer patient taking part in oncology drug research will have different preferences. Even the same patient may prefer different interactions at other times during the same trial.

FIGURE 3: SPONSORS AND CROS RECOGNIZE THE NEED TO MAKE TRIALS MORE PATIENT-FRIENDLY.

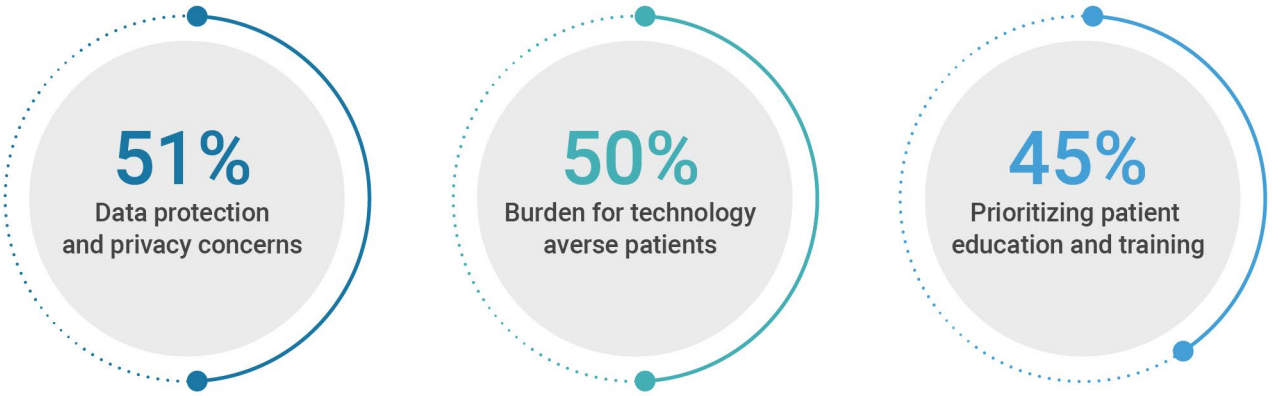



***Figure 3.*** *Sponsors and CROs recognize the need to make trials more patient-friendly. Sponsors and CROs reported that the biggest challenges with decentralized trials include data protection and privacy (51 percent) and the burden on technology-averse patients (50 percent). Nearly half of respondents (45 percent) are taking action to address these challenges by prioritizing education and training for patients participating in trials.*

Source: Veeva Systems

If they are not to add to the clutter of disjointed point solutions, patient-facing apps will need to be optimized for specific groups, based on disease, patient age, and other factors, yet fit into a holistic digital framework. Data protection and patient education will be crucial. The industry is still at an early stage in evaluating how best to approach this challenge.

In addition, human contact with healthcare providers will remain crucial throughout each study, ensuring a key role for sites well into the future. Studies designs will continue to incorporate multiple modalities for patient care—both digital and human—ensuring patient centricity and compliance.

## Closer Sponsor-Site Collaboration

Sponsors realize the need to reduce the technology burden on patients, and more of them are working to reduce that burden on research sites. Sites are crucial to trial execution and patient recruitment, especially as trial designs grow more complex. But sites' technology adoption has become an obstacle to clinical trial efficiency (**Figure 4**).

FIGURE 4: MORE SPONSORS AND CROS ARE REDUCING THE TECHNOLOGY BURDEN ON SITES.


***Figure 4.*** *More sponsors and CROs are reducing the technology burden on sites. 70 percent of sponsors and CROs report that site technology adoption is their biggest challenge with decentralized trials. Most (60 percent) have made the area their top priority for improvement, focusing on adopting a site-centric approach to their technology.*

Source: Veeva Systems

In their quest for more efficient digital applications, some sponsors have inadvertently made it more difficult for sites to focus on patients by requiring that they work with custom tools. As a result, the typical research site currently uses at least 12 different systems[3] to collect and capture clinical trial data, resulting in a proliferation of customized point solutions. A recent survey of research site leaders found that only 5% of available technology meets sites' operating needs very well.

One key to driving better sponsor-site partnerships is empowering sites with technology that meets their specific needs and makes it easy to share information. The industry has a long way to go in this area, but progress is being made as 60% of the CROs and sponsors say they are taking tangible steps to reduce site burden by improving data sharing and systems interoperability.

## Speed Bumps and Rising Expectations

At this early stage, companies working with decentralized trials acknowledge the challenges ahead, with 99% pointing to technical and operational difficulties. In addition, less than one-third have seen decentralization reduce trial costs or timeframes, while half of the respondents saw that decentralized trials imposed greater technology burdens on some patients.

[3] BioSpace, New CenterWatch Inc. Study Finds That E-Clinical Technologies Are Increasing Investigative Site Work Burden And Performance Inefficiencies, 2016

## Laying the Foundations for Change

Long term, experts say that industry-wide data standardization will be needed, not unlike the system developed for online banking, to create the digital infrastructure required for life sciences research. Within each company, procedures and workflows will need to be updated, and new SOPs created for processes that haven't existed until now. These efforts will require closer collaboration between sponsors, CROs, and site partners, who must agree on designs, tools, and processes, and share information. Recent surveys suggest that sponsors are already laying the foundation for this work, as a growing number of R&D leaders invest in EDC, eTMF, and CDMS.[4]

## Data: The Final Frontier

On a more fundamental level, companies will also need to tackle digital data optimization, an invisible, back-end challenge that often gets drowned out in discussions of patient centricity. Nearly half of sponsors and CROs noted the difficulty of collecting and reporting data.

As modern digital clinical trial designs evolve, there will be an urgent need to collect, ingest, aggregate, and clean higher volumes of disparate data from many more sources, including patient-facing apps as well as medical monitoring devices. Currently, this work must be done manually by teams of experts, requiring significant time and resources that would be impractical, if not impossible, to devote to each trial within each company's clinical portfolio.

Clean and standardized data will be crucial to making clinical research more agile and enabling more advanced approaches such as artificial intelligence in the future. Several companies, including GSK and Eli Lilly, are working on clinical databases that would speed data cleaning and standardization to allow the data to be managed, reported, and analyzed more quickly.

Although challenges remain, the industry is applying advanced approaches to manage and share clinical data and documentation as it redefines clinical trials and brings them into the digital age. Sponsors are also developing a better understanding of patient and research site needs and strengthening connections with both groups, resulting in a more sophisticated approach to patient centricity.

The goal for digital trials is a holistic platform that connects sponsors, sites, and patients for seamless execution and data flow to meet their diverse needs. Currently a work-in-progress, this platform would reduce trial costs and timelines by 25%. As it moves from concept to reality, clinical operations promise to become more innovative and better serve patients by speeding their access to medical breakthroughs.

[4] Clinical Leader, Rethinking Clinical Trials for the Future, 2021

Applied Clinical Trials

ARTICLE 3

# Data First: Building a Foundation for Digital and Decentralized Clinical Trials

By Richard Young, Vice President, Vault CDMS at Veeva Systems

Innovation and adaptation around COVID-19 restrictions have brought a "can do" spirit to the industry, particularly in clinical trials. This led to an increase in adoption of decentralized models that allow patients to participate in trials without repeated site visits, offering sponsors a way to increase enrollment and prevent attrition.

But the buzz surrounding patient centricity and decentralized trials has drowned out an inconvenient truth. Sponsors have no clear-cut way to aggregate and review the huge volume of patient data being gathered from disparate sources. This problem is not new - the industry has been working with decentralized trials, in some form, for over a decade. And looking ahead, to truly run a connected and digital clinical trial that enables decentralized approaches, companies will need complete and concurrent clinical data.

Sponsors may be able to capture patient data remotely and in real-time, but they cannot verify and reconcile it in anything close to real-time. Instead, most organizations use tedious, manual methods to aggregate and clean each silo individually (**Sidebar 1**).

We've heard from one Top 20 sponsor that, for a single trial, such efforts required 27 people working in shifts, 24 hours a day, for six weeks. Considering that most big pharma companies run hundreds of trials each year, the time and costs required to do this for every trial are prohibitive.

## An Explosion in Third-Party Sources and Non-Static Formats

The roots of this problem go back to the earliest days of traditional electronic data capture (EDC), where we saw data sources fragmented and isolated as we opted for speed of collection and sacrificed speed of analysis. With novel trial designs creating a drive for faster decisions, the ongoing explosion of data required for both traditional and decentralized clinical trials is changing our thinking. Today, a typical Phase III trial uses close to 10 data sources and generates an average of 3.6 million data points, three times the level that was seen 10 years ago.[5] One study found the cost to support data transfers between systems or companies in life sciences is $156 million annually.[6]

[5] Tufts CSDD Impact Report, Rising protocol design complexity is driving rapid growth in clinical trial data volume. Volume 23, Number 1, 2021

[6] Liaison Healthcare Informatics, Managing and Integrating Clinical Trials Data: A Challenge for Pharma and their CRO Partners

## SIDEBAR 1: DATA CLEANING: AN EXPENSIVE, MULTI-STEP PROCESS

To ensure the completeness and veracity of clinical data, information from each system must be reconciled with what's expected, which is typically maintained in the sponsor's EDC. Cross-checking data helps ensure expected data has been received, for example, that Patient A had his first blood draw on a specific date.

Safety and adverse event data are some of the most important and challenging data to review since multiple systems and time points are likely involved. In digital and decentralized trials, data is also reconciled to provide a complete picture of the patient status and procedures, as similar data is likely sourced from multiple systems.

Typically, to compare data sources, a listing is generated for the data manager to analyze. First, the data files are exported from the source systems and loaded into a SAS statistical software suite where a programmer performs the necessary transformations to compare the two. These transformations can be complicated as each system has its own data model and the mappings can be difficult to establish.

The programmer will then create and run reconciliation reports to identify discrepant data such as inconsistent dates or procedures, or duplicate data. They will export the listings, typically as Excel files for the data manager to review. When discrepancies are found, the data manager will write up queries, either within the EDC, within the source system, or manually via email. Considering the vast amount of data generated in today's trials, it is easy to understand the scale of the burden. It is not just effort and cost, but also time that makes this a fundamental challenge for our industry. //

Increased use of third-party data sources and non-static patient data have added complexity. Where, 10 years ago, most key clinical data came from physicians and was stored in the EDC, only about one-quarter of that data is now stored in the EDC. The remaining 75% — third-party data from smartphones and other sources — is managed independently and must be reconciled against the EDC. More and more frequently we see primary efficacy and safety data coming from outside of the eCRF, creating increased pressure on data integration strategies.

Further complications are introduced by non-static data formats, such as readings from wearable devices and monitors. Data formats differ between different systems, even for the same type of data - patient heart rate, for example. If measured via a stethoscope in the clinic, it will be recorded as a single data point, but a wearable device will produce continuous, high-frequency data. In the end, huge volumes of data collected at different frequencies will need to be managed, reconciled, and interpreted.

### The Added Complexity of Digital and Decentralized Trials

With decentralized trials, data that was once solely collected at the site may also be collected during telehealth visits, in-home visits, through ePRO apps, and more, each creating its own silo. Frequently, these scenarios require additional systems to collect the data and one size rarely fits all.

To get a clear view of the patient, this data must be aggregated and harmonized. For example, to see a patient's heart rate, there are multiple places to look—the EDC, the in-home visit log, or the iWatch reading. The source for each patient can also vary by visit—a trip to the clinic one day and an iWatch reading the next.

The same data is collected by different systems, at different times, and structured in different formats for decentralized trials, which makes synchronization significantly harder. This makes traditional data management capabilities such as querying important, yet it is not included in newer data collection tools.

One sponsor shared the challenges it faced after installing a system designed to handle patient data from remote nursing visits. The application did not include a querying tool. As a result, when data discrepancies emerged, the company faced three ugly choices: querying the data via email outside of the system; re-keying the data into its EDC; or paying for an expensive one-off integration. As this example illustrates, sponsors need an infrastructure that brings data together in an effective and scalable way.

When trials are fully digital with no paper, sites must use eSource, and an incremental challenge emerges. In these cases, data are not anchored to an EDC, which has traditionally served as the backbone for trial data, providing a reference point for other sources to be checked against. In a world of eSource that is managed by sites and where practices vary by site, working without the EDC means losing a fixed anchor against which to reconcile data. As a result, the data is much more difficult to clean.

When eSource and EDC co-exist in separate systems, sponsors must bear the enormous effort and cost required to reconcile the two. What will happen when we create truly patient-centric processes, whereby the patient will decide which visit they attend in person, versus perform remotely?

Mixing and matching at the data point level will become the norm, and current linear solutions are not designed with that in mind. Add to that the impact of protocol amendments and adaptive designs, and the conclusion is simple: companies can make it work for their important trials, but costs are prohibitive for the average study.

An integrated platform that connects the patients and sites with the sponsor's infrastructure for one point of cleaning and review would eliminate many of these challenges. Unfortunately, such an infrastructure doesn't yet exist, although many technology providers are working to deliver such solutions.

## Time Lag Prevents Data-Driven Decision Making

In decentralized trials, the time lag between data collection and the availability of clean data makes it more difficult to make informed decisions during the trial. Many new data-collection instruments are stand-alone tools that lack data review capabilities. When data needs to be reviewed, it must be transferred to the sponsor or CRO and imported into a separate system. When discrepancies are found, data managers must resort to disconnected email exchanges to issue queries, adding further delays and more manual work.

In 2020 and 2021, after COVID-19 restrictions took effect, some pharma companies invested considerably in decentralized trial technologies, only to find themselves with data that could not be connected or verified. They've waited months to extract, clean, and reconcile it with their EDC data, finding unexpected anomalies, such as different dates for a patient's adverse event. There has been no easy way to query data sources and ensure validity.

Delays viewing the data prevent trial practitioners from making data-driven decisions in a timely manner or being able to assure regulators that the data represents a completely accurate account of each patient's experience. For example, investigators may need to determine why a sensor reading appears out of range, such as when one patient's blood pressure suddenly spikes. Currently, there is no rapid way to verify these type of root causes.

*Standardization is very important if you want to simplify trials. Right now, you have 10 to 15 different external data providers, and everyone uses a different way to ingest data.*

— Mayank Anand, vice president and global head of data strategy and management at GSK

Consider a rare disease trial where each patient's outcomes are potentially meaningful to the others. If one patient's diagnostic readings trigger a change in the treatment plan, sponsors should be able to make that change instantly. If there is a delay before the data can be cleaned and checked, it leaves them liable for failing to stop potentially harmful treatments.

Establishing end-to-end data flows will be crucial if decentralized trials — and not just data collection—are to run in real-time. Not only will it be key to clinical trial agility and ensuring the validity of results, but it will also be a pre-requisite for adaptive trials.

Ironically, the industry's push for clinical innovation has only compounded the data management challenge. New technologies are being overlaid on a data management foundation that hasn't changed in decades. Designing a trial that is adaptive, digital and connected, and allows for decentralized execution (all in one protocol) with systems and solutions that support it must be the long-term goal.

## Standards Help but Will Never Fully Solve the Challenge

There is a clear and understandable desire for greater development and use of standards to address challenges. The industry has spent over a decade working to define data standards, yet still struggles with overall diversity and complexity.

"Standardization is very important if you want to simplify trials. Right now, you have 10 to 15 different external data providers, and everyone uses a different way to ingest data. Imagine what happens when you move to 20 or 30 different data sources. How will you standardize that data?" asks Mayank Anand, vice president and global head of data strategy and management at GSK.[7]

But there is no easy way to standardize. The needs for standards are diverse, and there are different standards for how data should be collected, moved, analyzed, and submitted. In addition, the clinical environment is dynamic: data changes; needs change; the understanding of science, and the human body, changes. Considering the pace of innovation in life sciences and the speed at which new data sources are introduced, it is not realistic to rely solely on standards.

[7] Applied Clinical Trials, Addressing Digital Trials, 2021

## SIDEBAR 2: BUILDING A STRATEGY FOR DIGITAL TRIAL DATA

**Life sciences companies are addressing the data challenge head-on. As sponsors develop their data strategies for digital and decentralized trials, we recommend informing the discussions by asking a few difficult questions:**

- **How easily and quickly can third-party patient data be verified?**
- **How much are we spending on data aggregation and cleaning, and what are we doing to simplify the process?**
- **Is there top-down commitment and real investment in clinical data management?**
- **How much would data management tools cost compared with the cost of trial failure or regulator's rejection of the application?**

**Failure to consider potential costs and 'what ifs' can only result in missed milestones. If they aren't addressed, they could hamper promising patient-centered trial approaches before they have even had a real chance to prove themselves. //**

### The Path Toward Complete and Concurrent Data

Company strategies for digital and decentralized trials must incorporate plans to connect the myriad sources of patient data into a single clinical data management system. With decentralized trials, the same data for different patients will be collected in different ways. Aggregating data in a central clinical data management system (CDMS) is crucial to achieving the visibility and timeliness that we know contribute to more effective trials.

Technology providers are exploring different ways to achieve this connection, but some options scale better than others. One approach is to use a clinical database or data workbench that stores clinical data in one place, allowing it to be cleaned and harmonized.

Veeva is working on such an approach, Veeva CDB, with several of the top 20 pharma companies. Veeva CDB includes a data lake that holds disparate datasets in their native structure.

These datasets are mapped to the study backbone using five metadata fields as a simple "key," rather than requiring a complete mapping, transformation, or adherence to a standard. This auto-mapping helps make data for the same point from different sources more equivalent (e.g., a blood pressure reading from a site visit vs. one taken from a device at home). Data can be ingested, aggregated, cleaned, and made readily accessible to other stakeholders in the organization.

One thing is clear, sponsors seeking decentralized data collection on the front end need centralized data management at the back end to prevent fragmented, heterogeneous data from slowing trials down. Automating the ingestion and harmonization steps will eliminate the time lag between data collection and access to clean data. Aggregating and cleaning sources simultaneously also address the need for patients to be treated consistently. For example, patient data from digital sources do not receive preferential treatment, which could otherwise result in questions of bias.

An additional approach to this problem will be to unify EDC and eSource solutions so that they capture data into the same system, which would allow data queries to be handled via EDC tools (**Sidebar 2**). Sponsors should also consider the benefit of having a single platform and data model extending from the patient to the sponsor. These requirements leave data experts with a strategic question: should they extend patient-facing data collection tools into the sponsor data environment, or move in the opposite direction?

Whatever approaches are used in the future, the industry clearly needs to make it easier to work with external data. "Pharma is already struggling to manage the volume of data we have for trials today," said Anand. "Over the next few years, as the speed of data ingestion increases, the industry will expect clean data output to be faster too."

*Failure to consider potential costs and 'what ifs' can only result in missed milestones. If they aren't addressed, they could hamper promising patient-centered trial approaches before they have even had a real chance to prove themselves.*

— Richard Young, vice president, Vault CDMS, Veeva Systems

ARTICLE 4

# Clinical *Kaizen* at Bayer: Moving Past Spreadsheets to Unify Operations

**By Jim Reilly, Vice President of Vault R&D and Quality at Veeva Systems**

Bayer is taking decisive steps to modernize clinical operations and move to unified digital clinical trials. Leading efforts to eliminate silos, streamline processes, and improve connections with Bayer's research site partners around the world is site management team leader Emma Earl, a 2021 Veeva R&D Hero. Through her efforts, the company is developing a culture of continuous, incremental improvement, or what Japanese business strategists have long called *Kaizen*, in its clinical operations.

Emma began her career at Bayer 22 years ago, and now heads a global team that works closely with technology vendors and manages global networks of users, applying both systems and process know-how to improve operations.

Emma also manages integrated processes across systems such as Bayer's site-monitoring system, which accounts for 30,000 reports each year, in one of Bayer's CTMS systems. "In a non-standardized world, getting sponsor companies to do things the same way is difficult," she says. Emma sees this as an area where modern, unified processes can add long-term value. "Shaving even 20 seconds off a process step that is used by over 1,000 employees makes a big difference. All the little steps add up," she explains.

## Change Management a Top Challenge

Although the industry is moving to digital processes, clinical trials have long been synonymous with paper. With a modern eTMF and purpose-built study startup systems in place, change management is the greatest challenge facing Emma and her team. "You can give somebody the best tool in the world, but if they persist in trying to work around it, you won't realize the efficiencies it was designed to give. Trying to get people to come along with new approaches is hard work," she says.

*Shaving even 20 seconds off a process step that is used by over 1,000 employees makes a big difference. All the little steps add up.*

— Emma Earl, site management team leader, Bayer

New tools are intuitive and have great search capabilities, she says, but their power also presents users with different choices. "Paper may have been tedious, error-prone, and time-consuming to work with, but its associated work processes were simple, well defined, and flexible. For some first-time users, 'decision paralysis' can set in when they have to set boundaries around work processes," Emma notes.

In addition, the people most affected by change aren't always on the receiving end of its benefits — at least, not initially, Emma explains. There is a need for users to see a much bigger picture. "They have to understand that they will be entering data into a system that offers more overall transparency and visibility across functions and users, and also supports multiple purposes," she says.

As Emma's team moves from data repositories to active data systems, it is trying to eliminate trackers, so that data are entered directly into one system. With previous legacy systems, every team had its own study SharePoint and their own spreadsheets, resulting in two or more filing systems to maintain. Many individuals are spending one to three hours a week just to update trackers, Emma says. Old habits die hard, and some will continue to use spreadsheets, even though every data point is already entered, and updated automatically, in the new system.

"Until we can get teams to relinquish control of those trackers, some users may see the new systems as requiring more time, when they actually save time," she says. At this point, Bayer's first clinical trials using an advanced study startup system just completed first patient enrollment, so it is too early to have any success metrics to share yet. Emma expects to start seeing benefits once more people become accustomed to working with the new tools.

To help with change management, the team sends employees updates via newsletters and a SharePoint system, as well as through change ambassadors and specialists. "The information is there, but the bigger task is to move people to it," she explains. "Study startup is especially complicated, particularly when the concept of trial milestones are new to all. 'Expected documents' was a term that many of them had never heard until last year," says Emma.

## Working with Research Sites: Making Technology Their Choice

But change management also affects users outside Bayer. With Veeva Site Connect, for example, timing implementation at research sites is a major challenge. "Site study teams are under intense pressure to start up studies as quickly as possible, and it complicates processes when you introduce new technology at this point," Emma says. Finding the optimal timing to increase site engagement is challenging. If following study-specific outreach, then engaging sites too soon and before selection is not ideal, as it can give a false impression of successful site selection.

Nevertheless, Emma sees the use of flexible site connectors as a major improvement over traditional sponsor portals, which are complex and may require multiple integrations. Besides, some research sites simply refuse to use anything branded as a portal, while others want to use their own electronic Investigative Site Files. "Making technology the site's choice is important," Emma says.

Bayer is still on a learning curve with its digital technologies, but Emma expects them to aid standardization, boost efficiency, and show sponsor consistency, which is important to sites. She also sees standardization improving the speed and quality of trials, for instance, by allowing trial documents to be reused for similar studies to prevent teams from having to reinvent the wheel. Emma's next goal is incorporating more visibility into its new business tools so that decisions become increasingly data driven.

### Connecting with Regulatory and Safety

Looking ahead, Emma and her team are working on establishing stronger connections between clinical operations and Bayer's regulatory and pharmacovigilance operations.

"Cross-functional communications have led to some tough conversations and questions, such as 'Where should that document live, and who does it belong to?' but we're able to work those issues out together, to find the best path forward, and think of the overall impact, rather than each team focusing on [maintaining] control," she comments.

"Getting users to see the big picture is a work-in-progress," Emma says. Day by day, her team's efforts are establishing the foundations needed for more efficient clinical operations, as they convince more users, inside and outside the company, of the benefits and the need for change.

## Conclusion

The clinical trial operating model is evolving as the industry embraces new, more connected ways to conduct trials for greater efficiency, high-quality data, and improved stakeholder engagement. Changes are underway that will streamline study execution, simplify information sharing and collaboration across stakeholders – and ultimately, get safe and effective treatments to patients faster.

See how LEO Pharma is advancing its clinical trials to deliver a better patient experience and speed the development of innovative treatments.

Veeva

**About Veeva Systems**
Veeva is the global leader in cloud software for the life sciences industry. Committed to innovation, product excellence, and customer success, Veeva serves more than 1,000 customers, ranging from the world's largest pharmaceutical companies to emerging biotechs. As a Public Benefit Corporation, Veeva is committed to balancing the interests of all stakeholders, including customers, employees, shareholders, and the industries it serves. For more information, visit veeva.com/eu.