EDETEK

Transforming Data Into Assets

The Digital Clinical Trial: An Ecosystem View

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Executive Summary

Ten or fifteen years ago, the concept of the digital clinical trial was very different. It was merely a notion, a theoretical and somewhat abstract idea that was narrowly and differently defined by every department or functional area that was involved in the clinical data lifecycle. There was no cohesive understanding of the concept and most people duplicated existing silos of activity and information into their interpretations. The concept was more of a vision for a future state than anything grounded in practical experience.

Fast forward a decade or so and we see a very different landscape. Cloud technologies have democratized access to data. New sourcing and partnering strategies have resulted in dispersed team members and systems, all over the world, requiring seamless standards-driven data integration, access to systems, data and metadata as well as visibility into associated processes. Clinical and operational innovation have changed the way we work and it is about to happen again.

The digital clinical trial is no longer an aspirational thought. However, there are still very different interpretations of its applicability, the breadth of its reach and the transformational impact it can have on stale, outdated processes.

This paper will attempt to highlight the emerging potential of the digital clinical trial and in the process, help to illustrate its broad reach and impact on clinical research.

Traditional Drug Development

Drug development is a costly and complex process. According to PhRMA, annual spending on R&D in 2015 was approximately $58.8B[1]. Roughly 48.3% ($24.8B) was spent on clinical trials[2]. Within the clinical trial, a great deal of time is wasted looking for study events, issues and data patterns across systems instead of reacting to these events. For example, manually exchanging data or using cumbersome procedures and devices that require additional work and time delays cost Life Sciences companies billions of dollars each year in delayed decisions and process inefficiencies. Manual approaches to addressing these issues have proven costly and have added resource time while also introducing another opportunity for human error. There are no continuous quality evaluation instruments that can ensure the continuing health of the trial as well as patient safety and regulatory compliance.

A New Perspective

It is helpful to look at the digital clinical trial as a collection of activities and events, data, metadata, medical professionals and patients, issues, systems and processes that are connected through an information hub. It is a dynamic ecosystem where GxP requirements, data standards, regulations and best practices influence the path from planning to data collection to inclusion in a regulatory submission to health authorities. This broader view of the digital clinical trial rests on the following assumptions:

- Metadata, or data about the data, can be leveraged to streamline the flow of data through myriad processes including collection, review, standardization, analysis, regulatory submission and

[1] PhRMA Profile 2016

[2] EFPIA Website; PhRMA Annual Membership Survey 2016

warehousing for future use cases while simultaneously facilitating *continuous* information quality and ensuring consistent interpretation of the data throughout those processes.

- An information hub approach enables connectivity and integration of all systems exchanging clinical information while information exchange rules ensure data privacy, security, appropriate formatting, validation, and guaranteed information delivery.
- Event-driven or reactive activities can be automated thus strengthening the entire system.
- Resources (people and systems) require various levels of access/visibility into the ecosystem in order to process data and respond to events, activities or status changes.
- Clinical information (structured or unstructured) is readily available for study participants and their systems
- Compliance (GxP, 21 CFR Part 11, Annex 11) with all appropriate data standards, guidances and regulations must be enforced across the ecosystem.

This view of the digital clinical trial does not limit its potential impact to one particular task (e.g. data collection). Rather, it expands the potential effect with an inclusive view of the trial and all of its stakeholders. Patients, who have historically been excluded from ongoing clinical trial communications and information can now participate more fully in the process. Resources may come in and out of the clinical trial ecosystem at different times, requiring different levels of access and integration to complete required tasks. Their access to data may change at different points in the process. Their roles in the process may change and the data itself may change. This means that the collection of moving parts – stakeholders, data and activities - known as the digital clinical trial must take place in a controlled "system". There are several core capabilities that are essential to this complex system.

Connecting Data Producers to Data Consumers

The digital clinical trial may be optimized to ensure both efficiency and data integrity. But in order to do this, data producers must be linked to data consumers. Traditionally, these pathways are disjointed at best. Siloed departmental activities are limited by functional boundaries. These boundaries were probably initially built to protect the integrity of the data but now they pose challenges to the integrity of the process. They also create a scenario where there is a high latency of actionable insights coming from activities, negatively impacting the value of these insights from business and scientific events. In the new holistic view, even clinical trial participants can be both data producers as well as data consumers. Patients can now have a much richer trial experience based on bidirectional communication and make better informed decisions about their healthcare as active participants in the digital clinical trial.

In addition, sources of data continue to vary. With the increasing use of wearable devices and IoT (Internet of Things) in clinical trials, some of which are even BYODs (Bring Your Own Devices), vast amounts of data must be stored, processed, reviewed, analyzed and transformed in near or real time in a compliant and quality state. By enabling a tighter connection between data producers and data consumers, the digital clinical trial also enables a deeper level of collaboration across a broad spectrum of activities. The variety of clinical records may include output from EDC or EHR/EMR systems, trial management information from CTMS, IRT or Clinical Supply systems, serious adverse events, patient reported data, data standardization requirements, discrepancies and issues. Future digital trials will use systems that ensure the integrity of a variety of medical records with technologies introduced by blockchain, a decentralized digital journal that tracks transactions across many computers so that a record (block) cannot be altered retroactively without the alteration of all subsequent blocks.

The digital clinical trial demands a deeper level of data, process and system integration in order to ensure continued data quality. Within the ecosystem, stakeholders should be able to review data, identify and

remediate issues, finalize data sets and track approval processes – all while using integrated tools that function within the ecosystem and throughout the clinical data lifecycle. All of these activities and resources should be operating and moving within the same globally available and secure framework where data, published system interfaces and metadata help to connect participants across the clinical data lifecycle.

This view enables new stakeholders to participate in clinical trial communications. Renewed interest in acknowledging and hearing the patient voice is motivating sponsors to engage more frequently with trial participants in order to improve recruiting and retention. The digital clinical trial enables sponsors to do so efficiently and effectively by opening the ecosystem to this new segment of stakeholders where direct access to their relevant data is encouraged and supported.

The ecosystem approach also eliminates the need for sponsors to constantly integrate and coordinate information exchange. By capturing, storing and processing data in one centralized location, using integrated tools, sponsors can simply add new users and systems to the ecosystem as required. The significant burden of coordinating this information exchange can be passed on the ecosystem itself. Taking this scenario one step further, contract research organizations and development partners can "digitally connect" with sponsors without requiring time-consuming and expensive data and system integration projects. Nearly 80% of all clinical information and 100% of operational data can be automatically received from digital sources and vendor systems. This represents a substantial time and resource savings that can be replicated for each clinical trial and directly results in decreased clinical trial costs. Additionally, digital trial participants can re-use the interface while serving different pharmaceutical sponsors, thus decreasing the cost of services and improving data exchange consistency.

Around the Clock and Around the World Accessibility

The digital clinical trial never sleeps. With global participation, clinical research and access to clinical data is continuous and must be “always available”. In today’s fast-paced clinical trial ecosystem, time zones are almost irrelevant. With the advent of cloud-based technologies that can be accessed anywhere in the world with an internet connection, this has never been truer.

Cloud computing has fueled the demand for data accessibility. It has also fueled the need for greater oversight into ongoing clinical processes. Outsourcing processes to Contract Research Organizations (CROs) is a common strategy for clinical trial sponsors who require additional resources or specific knowledge or skill sets. Sponsors who outsource portions of a clinical trial must maintain a level of oversight to ensure the integrity of the trial and the science as required by ICH E6 R2. Cloud computing technologies such as a clinical information hub and clinical data lake enable sponsors anywhere in the world to collaborate with vendors and study patients and monitor their activities to ensure compliance, meet contractual obligations and ensure the quality of the data and supporting processes.

The dynamic and reactive (event-driven) nature of this environment enables a new level of flexibility, changes and responsiveness. This level of accessibility also helps to efficiently manage issues from identification through resolution.

Compliance

The digital clinical trial must maintain compliance. GxP rules, regulations and guidances, such as ICH E6 R2, apply to activities throughout the clinical trial. Because it is now taking place in an electronic ecosystem, 21 CFR Part 11 Compliance is required for all digital components. Validation of the system and supporting processes is important to ensure continuous performance and that it operates as expected.

Geographical compliance is also an important aspect of the digital clinical trial. As clinical trials increase in complexity and expand to new populations around the world, it is important that the ecosystem address regional and local compliance requirements such and the EU-US Privacy Shield that protects patient information. Japan is another example of a region where the expanding scope of privacy laws are enforced to protect confidential patient health information.

Robust Toolsets

The ecosystem approach to clinical trials requires that process participants have access to powerful tools to exchange, review, manage and transform data within its secure and compliant environment. Tools that automate quality processes based on key events, enable deeper partner collaborations and improve data quality become essential to the successful digital clinical trial. Over time, these types of tools become the recipient as well as the source of business and scientific insights that the team can quickly reinvest into the process.

Once all of the digital clinical trial information is brought into one ecosystem, it requires views that support various roles throughout the trial. Dashboards and powerful reporting tools will help to simplify data presentation and provide broader, more strategic views of the clinical trial portfolio. These views must support operational and tactical decision making while also providing higher level data-driven displays of status and progress.

Real-time aggregation of activities and events provides new insight into clinical trial processes. A meaningful presentation of this information that makes it not only consumable but also actionable, is essential. For example, if a patient consent form is signed, a sponsor may assume that data from the first patient visit can be expected shortly. If no data is received, the event becomes suspect. Just as expected data can trigger activities, lack of anticipated data can also trigger some type of follow up or workflow to

confirm that the patient is an active participant in the trial and all associated processes are being appropriately performed, thus ensuring continuous compliance and quality.

The Digital Clinical Trial Continuum

Small life sciences teams have very different needs than larger, global organizations. As small teams start first in human studies, their view of the digital clinical trial may only include electronic data capture. This is a great starting point for small teams, whether or not they are outsourcing all or parts of the study. Electronic data capture enables systematic cleaning and management of clinical data while reducing the human data entry burden and risk of error. Electronic health records and electronic medical records hold the promise of additional advances in automation of the tedious data collection, translation and cleaning process. As teams grow, they can expect to embrace a larger, more holistic view of clinical trials where activities such as data transformation by a partner or vendor are enhanced through collaboration and automation of template driven standardization tasks. Standards such as CDISC CDASH, SDTM and ADaM have matured to the point that many teams have gained valuable experience with them. Yet, they are not static rules and as they continue to evolve, and the nuances of best practices are being captured and documented. As teams collaborate with their partners to more efficiently implement the standards, their concept of the digital clinical trial and the ecosystem in which it takes place will again evolve. Finally, global teams who are working with multiple development partners and crossing geographic and organizational lines on a daily basis may have a much broader understanding of the digital clinical trial. They understand the importance of connecting data producers to data consumers, they do not underestimate the importance of data integrity and how and where it is ensured, they have bought into compliance as a priority and they appreciate the value of a centrally located “hub” where stakeholders and their systems can securely interact within the clinical trial ecosystem.

Recommendations

It is important to align the resources, capabilities and performance measurements of your organization with your business priorities. A clinical trial is a strategic investment. Taking a holistic view of the digital clinical trial will help your team to continuously use business insights to improve the clinical trial process while meeting your business goals.

Start to plan your digital clinical trial strategy by looking at data sources. Understand where data comes from, the format it takes, where it is stored and processed and what issues commonly arise. Invest in or subscribe to an industry leading information hub that either has “out-of-the-box” connectivity or is capable of adding your clinical trial data producers to connect with data consumers in a seamless manner.

Next look at the stakeholders in the process - who needs access to data and what type of access do they need. What are their biggest business challenges and how can the digital clinical trial address them?

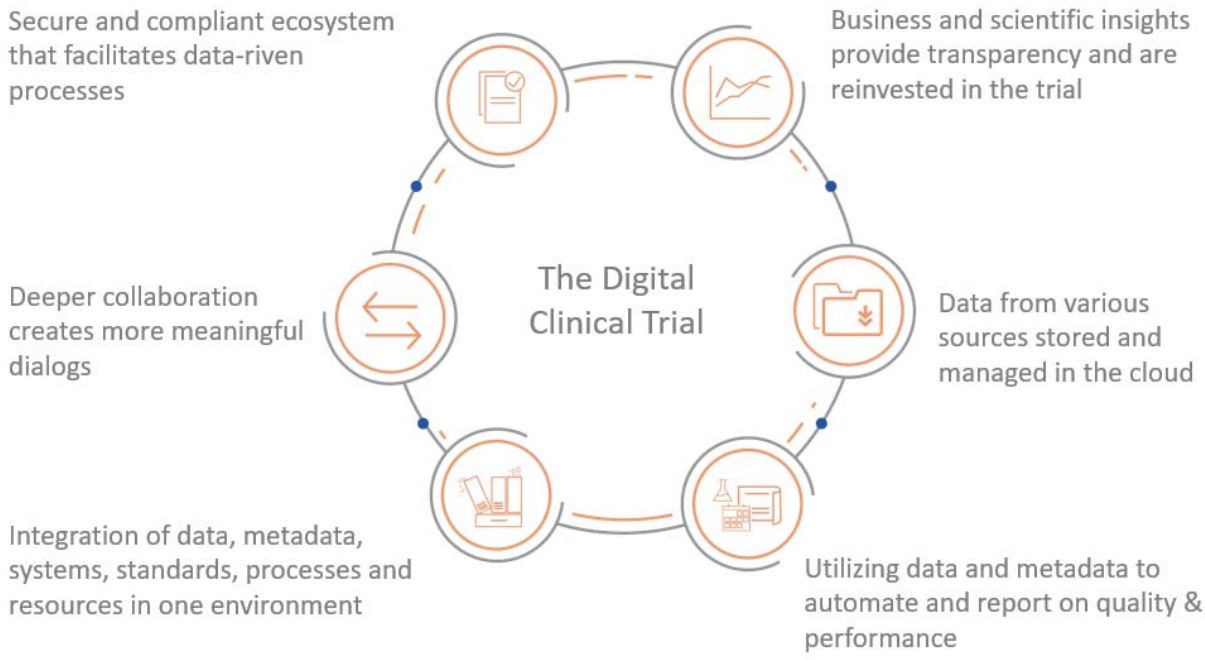
Consider how events and activities impact the clinical trial. If a particular piece of data reaches a certain point in the process, can it automatically be presented for review or can it’s finalized state trigger a data standardization template to be applied before it is officially approved?

These activities will help your team to begin the journey toward the digital clinical trial while enjoying the benefit of rich clinical informatics that are being derived from the process.

EDETEK’s Vision

The EDETEK team has developed a vision of the digital clinical trial that supports clinical research teams at whatever point on the continuum that they are operating. Our approach to the digital clinical trial is based on four foundational principles:

1. A digital clinical hub connects data producers and data consumers. Data quality and trial efficiency are directly related to the degree that these stakeholders are connected.
2. Standards, clinical trial metadata and best practices may be applied throughout the process in order to automate, track and expertly manage clinical trial deliverables.
3. Online collaboration, tasks, processes (and other digital activities) must be initiated and managed in ONE secure and compliant ecosystem.
4. The digital clinical trial ecosystem must be reactive, thus, constantly informing sponsors, patients and vendors about the data and supporting their role in the clinical data lifecycle.



This view of the digital clinical trial attempts to remove the barriers to progress that have been built into existing information silos. By creating a dynamic and supportive ecosystem that exists solely to support quicker, more efficient processing of data across the clinical trial lifecycle, we begin to move closer to fulfilling the profound vision for the digital clinical trial.

This holistic perspective requires a different, more strategic view of clinical trial applications, data and metadata as critical assets that require a balance of protection, collaboration and automation. This view can be directly tied to the company's strategic goals while still having a meaningful impact on tactical, daily operations. The digital clinical trial is a powerful concept that is now being used across the life sciences industry to transform the way teams conduct and manage clinical trial data and the broader clinical data lifecycle.

EDETEK is operationalizing the concept of the digital clinical trial. As Digital Clinical Trial Experts, you can look to us for additional content that articulates our commitment to developing powerful solutions that support the new digital clinical trial. Visit our website at www.EDETEK.com.

