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Data Management in the Face of Growing Trial Complexity

Vertex Pharmaceuticals leverages innovative processes and technology to help tackle the industry's toughest data challenges

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According to Tufts Center for the Study of Drug Development, the average time to build and release a clinical study database is more than 73 days and the average time to lock data at the end of a trial is nearly 39 days[1] – combined, this is more than five days longer than it was 15 years ago.[2] With increasingly complex clinical studies, the industry can't afford to go backwards. Study delays slow treatments to patients and can cost $1 to $13 million dollars a day.[3]

In 2017, Vertex Pharmaceuticals addressed this issue head-on by setting aggressive internal targets despite already outperforming industry averages for most data management timelines. Vertex implemented innovative processes and technology to tackle the industry's toughest data challenges, such as reducing turnaround times with central labs; integrating external data sources, gaining buy-in from sites and internal departments to the data review and lock process, and reducing excessive and lengthy rounds of UAT. The company has since reduced database build and release times from 12-14 weeks to six to eight, and data lock times from 22 days to just 15.

"You can't compress a 12-week timeline into six weeks just by working faster," said Vikas Gulati, executive director, clinical data management and metrics at Vertex. "Likewise, there is no benefit in shortening database build times if it causes you to extend lock times or impacts quality. We needed to fully rethink our capabilities and processes to uncover new ways to improve efficiency. In the end, we were able to shorten builds while maintaining quality and our rapid data locks. We also had to ensure if we can build faster, our central labs and IRT vendors can go equally fast to ensure medical monitoring and all systems go-live at first-patient in."

More Data, More Sources, More Stakeholders

The growing complexity of clinical trials has complicated data management processes in various ways. First, there is a greater volume of data in clinical trials. Overall, the number of data points has nearly doubled, from 494,236 in trials between 2001-2005 to 929,203 in trials between 2011 and 2015.[4] Sponsors and CROs report that handling today's high volume of data is one of the biggest challenges with data management.[1]

In addition to increased data volume, the number of data sources – including digital

sources and wearable devices – is growing. According to Tufts CSDD, the average number of data sources used in clinical trials will increase from four to six in just three years.[4] Vertex, for instance, uses on average at least six data sources.

For many organizations, a third complication impacting data management is the number of stakeholders involved. In 2019, about half of all clinical trials are outsourced to CROs – often more than one CRO per trial – and each have their own data management methods and technologies. While Vertex has direct access to their data, most sponsors are dependent on periodic data transfers from their CROs. Sponsor and CRO systems are typically disconnected from each other and from external data sources. With each additional source, data cleaning and access become more complicated. Internal stakeholders including safety, medical, and statistics, also need to review the data, further raising the stakes on securing timely access to all of the data.

Smarter Ways to Speed Database Build

Vertex began its journey by reviewing existing processes and technologies, and uncovered a number of opportunities to improve database build and release timelines. Here are three for consideration:

1. *Improve the efficiency of edit checks*

On average, clinical teams have 300 to 500 edit checks per study. Vertex was double and triple-testing each edit check across functional areas – essentially creating multiple, redundant layers of edit check verification. Vertex shaved time from this process by re-defining which teams test what edit checks and when. In addition, Vertex examined which data points merit User Acceptance Testing (UAT) and edit checks within its electronic data capture (EDC) system, versus those that can be reviewed and checked another way.

"Most edit checks never fire, so we took a more discerning look at our UAT process for edit checks," explained Gulati. "We can still ensure quality data while changing how we check low-value data points versus high-value or high-risk edit checks, and taking a risk-based approach rather than enlisting every team to review every piece of data multiple times."

Eliminating the review of low-value data points up-front, has helped Vertex employ a timesaving risk-based process to significantly increase process efficiency.

2. *Eliminate UAT of data elements from previous studies*

UAT is a necessary but time-consuming process. And while Vertex maintained an extensive standards library, the company would still need to perform UAT on 100% of the edit checks in each study because it couldn't verify that nothing changed from the previously-tested elements in the library. However, after Vertex adopted a new EDC solution, they received reports that show precisely what is different from one study to the next. Standards can now be validated once and re-used in other studies without additional UAT.

Vertex is working closely with its quality team to vet this new process. Once it has been validated and incorporated into their standard operating procedures, Vertex will only conduct UAT on new elements, further improving speed and efficiency. This process change will have a particularly high impact for Vertex as 90% of its trials are in one therapeutic area so re-use from its standards library is high.

"A key part of our approach to building studies has always been using standards. We have an extensive, well-governed library," said Gulati. "With our new technology solution, that library now translates into extensive UAT time savings. We can eliminate much of our UAT by only testing new data elements and those that

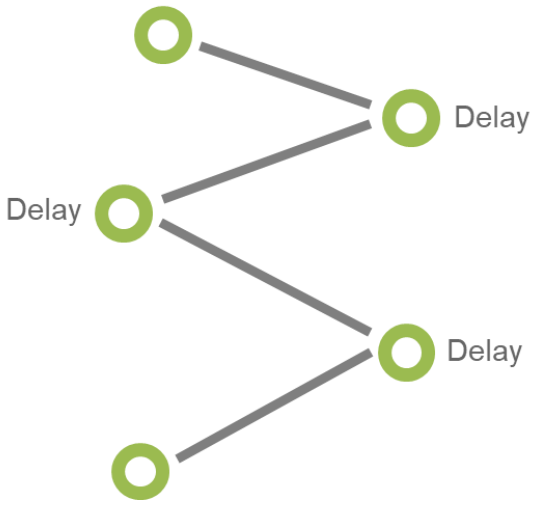
didn't have edit checks verified in a previous study."

3. *Move from ping-pong UAT to live UAT roundtables*

Traditionally, UAT is a multi-exchange back-and-forth process between the CRO and the sponsor. Internally, too, it can take many days to gather comments from the various stakeholders. In total, these ping-pong exchanges can take four to six weeks. Vertex replaced this cumbersome process with a live, roundtable-style approach to UAT that brings the vendor and sponsor teams together – either physically or virtually – for collaborative review. Both groups review and provide feedback in real time, and the system is updated concurrently. Vertex now completes the equivalent of three rounds of UAT in just two days.

"Live UAT updates is a game changer," noted Gulati. "By providing feedback, fixing problems, and testing updates immediately, we can eliminate three to four weeks from our timeline. This is a big departure from our current approach, but you can't make substantial improvements without substantial process and technology changes.

Current Ping-Pong Approach



Live, Iterative Approach

Real-time feedback, updates, confirmation, documentation

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- Vikas Gulati
Executive Director, Data Management and Metrics
Vertex Pharmaceuticals

Lock All Trial Data 30% Faster

The process of locking the EDC database confirms that all quality checks, cleaning, and query resolution are complete and prevents further changes to the data. It is also an opportunity for the data management team to directly impact clinical trial timelines and help speed medicines to patients. In order to reduce data lock times, Vertex emphasizes the importance of reviewing clinical trial data immediately, from the first patient screened, and continuously throughout the trial to be able to lock data right after the last patient visit.

"You cannot wait to start reviewing data until the three- or six-month mark," explained Gulati. "Reviews must start immediately, and across all teams. For example, we are not waiting for the CRAs to get to a site and confirm data is correct. We are reviewing and cleaning data on an ongoing basis."

Since 2017, Vertex has also worked to automate data collection from its primary labs. "We spent a great deal of effort creating processes and implementing technology to enable access to all data – even external data – very quickly and easily," added Gulati. As a result, Vertex has reduced its data lock time on ALL its data by 31% from 22 days in 2017 to just 15 days today, less than half the industry average.

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Sources:

*1. Tufts Center for the Study of Drug Development, Impact Report, Volume 21, #22, "Drug Development Outsourcing Outpaces Internal Spending," March/April 2019. See report **here**.*

*2. Tufts Center for the Study of Drug Development, "Industry Research Shows 97% of Companies to Increase Use of Real-World Patient Data for More Accurate Decision Making," November 2017. See full news **here**.*

*3. The Pharma Letter, "$1-$13 million a day at risk from product launch delays." May 2014. See the full article **here**.*

*4. CISCRP and Tufts Center for the Study of Drug Development, "Industry Practices That Will Benefit by Patient Engagement," by Ken Getz, October 2017. See full white paper **here**.*