Pharma Intelligence
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Decentralized Clinical Trials: Managing The Volume And Complexity Of Data

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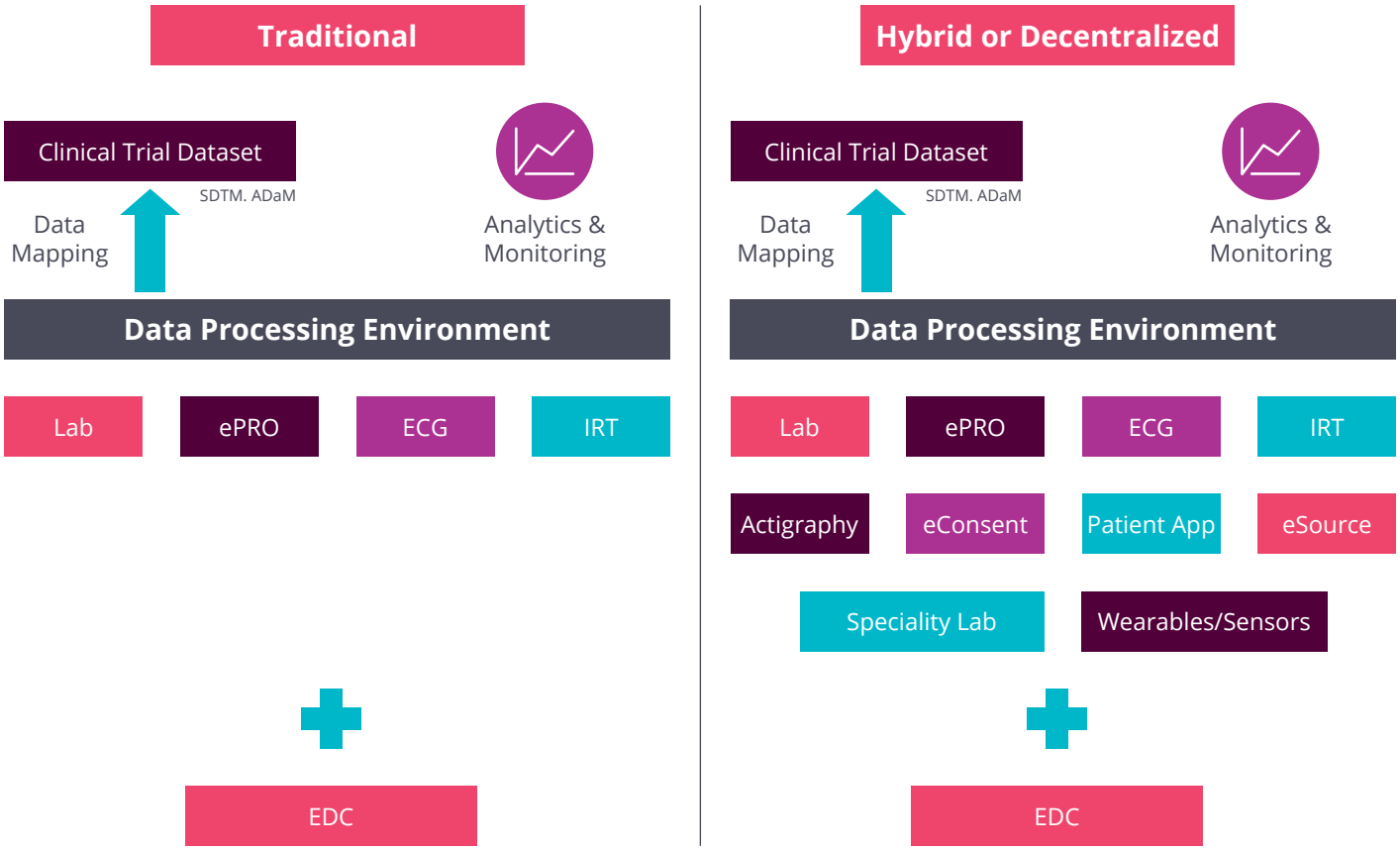
It is generally agreed that the pandemic accelerated the adoption of decentralized and hybrid clinical trials and according to many commentators they are here to stay. Many countries in Asia appear to be open to the use of these models, however regulatory authorities are looking to other regions to see how they are responding before issuing new guidance. Pharma and biotech organizations in Asia are looking to CROs for practical guidance on how to conduct these clinical trials and exploring what is possible in different countries. Anecdotally, it appears that investigative sites are already getting ready for the changes they will need to make to manage clinical trials that have decentralized components, such as some patient visits being conducted at home or in a convenient location.

Regardless of where the clinical trial is conducted, as the shift towards decentralized and hybrid clinical trials expands the number and variety of available data sources, the volume, diversity and complexity of accumulated data have increased in parallel. Source diversity enables treatment effects to be assessed from different perspectives and in different settings, with more emphasis on real-world quality-of-life measurements. Ultimately, it nudges the trial closer to how a drug might perform in a broader patient population.

These benefits align with growing demand for demonstrable value in healthcare systems, however they do not come without challenges. The sheer volume of data coming out of clinical trials is not new

Clinical Trial Dataflow: Traditional vs Hybrid or Decentralized Trials



but the range and heterogeneity of data sources, call for a whole new level of oversight. As Rhona O'Donnell, ICON's senior director, Data Management & Clinical Risk Management, explains these used to be limited, typically, to electronic data capture and anything from one to four other sources, such as laboratory and electrocardiogram data, interactive response technology and electronic patient-reported outcomes.

Decentralized trials add to that list data from specialty labs, from wearables and sensors, patient apps, actigraphy devices, eConsent processes and eSource systems.

As O'Donnell notes, each of these requires a distinct process to set up the source, deliver the data, perform integrity checks, and review the data against the sources. "And you still have to have all of this ready for when the first patient is in," she adds. "There's much more of a technical set-up, and much more planning is required upfront."

With established suppliers such as lab vendors, the process is facilitated by highly standardized data-transfer agreements, where "we know what data to expect", O'Donnell continues. With new technologies such as wearables and sensors, however, vendors may have less experience of clinical trials, requiring closer attention to issues such as data reliability and ease of integration.

Data Variability

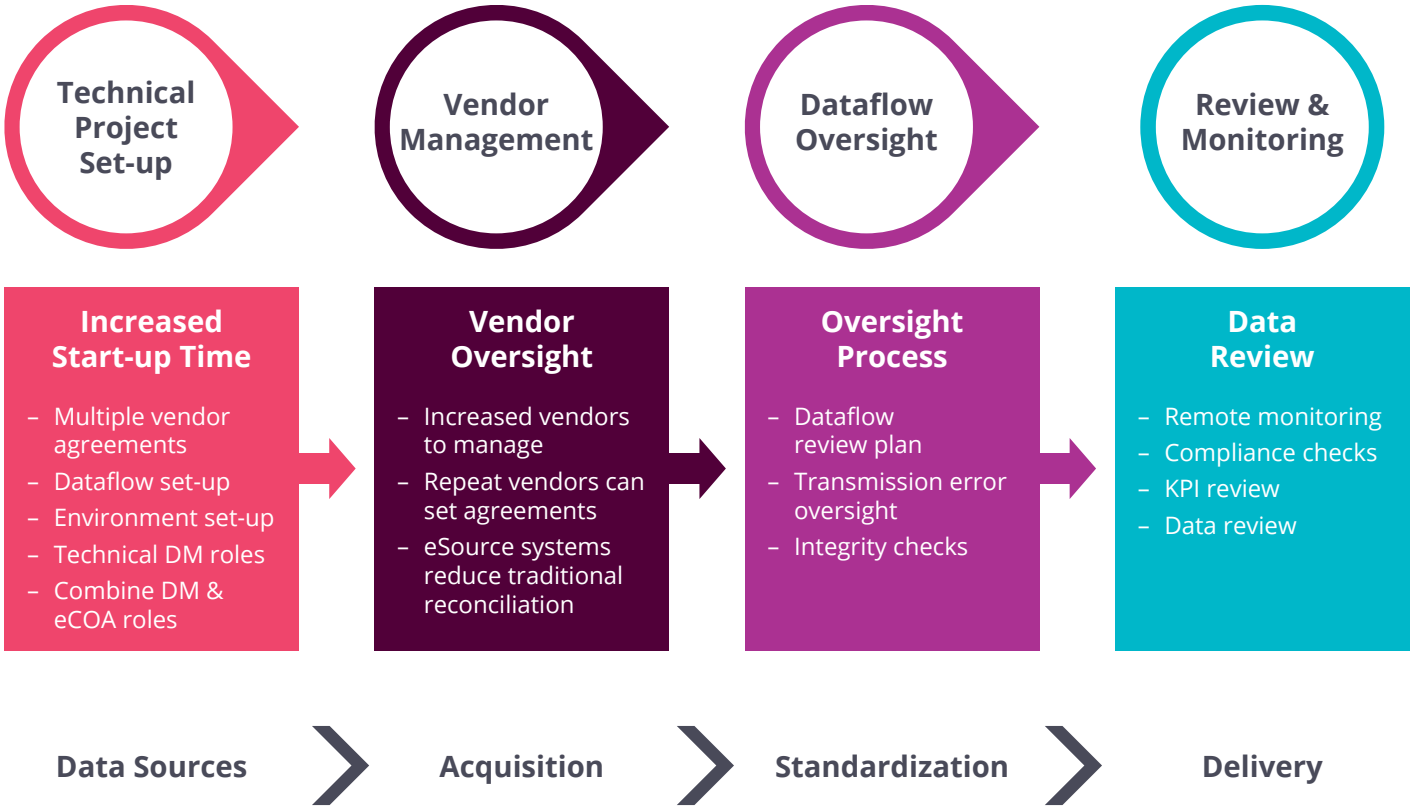
Moreover, observes Lalit Pai, senior vice president and head of Global Biometrics at ICON, the potential variability of data from a wider range of sources means the whole "data backbone needs to be more robust now". Those data may include patient-generated content from different types of devices, raising data-transfer, -anonymity and -quality questions while pushing up complexity levels.

These issues must be worked out with data vendors upfront at the protocol planning stage, O'Donnell stresses. For example, some vendors may collect "millions and millions" of patient records but provide only summarized datasets. With other vendors, "we are going to get all the records, and then we need to work out algorithms and how we're going to derive the information."

The same principles apply to ensuring the consistency and reliability of clinical trial data generated virtually, particularly when this is done on a bring-your-own-device (BYOD) basis. Again, it is about defining in advance the data to be collected, organizing data collection collaboratively with the provider, agreeing associated data formats, and conducting user-acceptance testing on data-generating devices.

Pai also emphasizes the importance of contextualizing data outputs. Each study is different, whether by therapeutic area or the way the data need to be interpreted. Using their subject-matter expertise and the company's ICONIK clinical informatics platform, ICON's data managers can identify patterns in data from multiple sources and "look at things that don't appear right", Pai explains.

Adapting Roles and Processes for Decentralized Trials: Data Management and Clinical Operations



Traditional Process	Decentralized Trial Process
Data Reconciliation	Data Integrity and Compliance Checks
On-site Monitoring	Remote and Central Monitoring
Data Cleaning	Data Issue Review and Resolution
EDC Data Entry	eSource + EDC
1-2-1 Data Mapping	Multi-source Data Mapping

Traditional Role	Decentralized Trial Role
Data Manager	Technical Data Manager/ Data Scientist
Data Reviewer	Combined Data Manager, Data Reviewer and Central Monitor
On-site Monitor	Remote and Central Monitors
Project Management and Vendor Oversight	Project Management and significantly increased vendor oversight

It is important to define the process and agree responsibilities in the planning stage.

Data Review Parameters

Another important step during study set-up is defining the parameters for data review. This means drawing up a coordinated plan that establishes the various roles of medical monitors (reviewing data from a medical perspective), data managers (reviewing consistency/ cleanliness; looking for patterns in the data) or clinical data analysts (looking for outliers and trending; providing feedback to sites on data quality).

Standardization across portfolios and the industry would be a great help in this respect, Pai adds. In some areas, customers may be looking for more data variability to provide richer insights. However, breaking the mold in every data domain "is not really necessary", Pai insists. Better to have the right balance of standardized and non-standardized data, generating real value while facilitating activities such as downstream processing.

There may also be challenges around connectivity and device malfunction in trials relying on mobile technology "I don't think any electronic clinical outcome assessment (eCOA) device is going to function 100% perfectly," O'Donnell comments. Moreover, when eCOA is used for patient questionnaires or eDiaries, these are contemporaneous data. If they are not collected at the time, "you can't look back and decide how you felt two days ago".

Device Level Management

As Pai notes, much of this comes down to data management at device level. Each app will have an administrative layer or 'overhead', consisting of, for example, a function that logs every keystroke or data transfer. App and device companies need to consider the amount of overhead they incorporate (increasing required system resources and slowing down performance) in relation to the volume of data they want to capture.

"Without a certain minimum level of data logging, we will not allow the eCOA or app vendor to go ahead with the trial," Pai comments. If an issue such as device malfunction results in data loss, then without an acceptable degree of data logging, data managers risk being left high and dry.

Data privacy, security and anonymity are also issues that require early risk assessment to identity and pre-empt any potential vulnerabilities and country specific requirements. As O'Donnell explains, there are already strong protections in place with more traditional EDC, IRT or test laboratory systems.

Data are anonymized with no central decoding key, and only the trial sites know the patient identifier. With newer vendors, though, such as BYOD of eCOA providers, more effort may be needed to ensure the necessary firewalls are in place and anonymity is watertight.

Data integration is one more challenge amplified by the proliferation of new data sources. As soon as data are collected, they must be integrated and surfaced through the ICONIK platform, so that useable data are available both to sponsors and all the relevant teams within ICON. Here again, newer sources such as sensors or wearables may be more problematic, due to volume or variability in data formats and the data themselves.

Advanced Analytics

Technology and analytics capabilities have evolved along with the expansion of data sources in clinical trials. It is not just about surfacing and aggregating the data but generating more sophisticated visualizations as a basis for meaningful extraction and observation. At the back end of the operation, Pai adds, more advanced project-management and data integration skills are needed to handle inputs from new data vendors. Consumer device companies, for example, may not understand so well the necessity for data validation or retention.

For service providers addressing the challenges of multiple data sources in decentralized trials, the immediate pay-off is accelerated data flow directly into data integration systems, rather than relying on trial sites to input data in their own time. With newer sources such as eCOA, wearables or sensors giving real-time access to data, "we can review these more quickly and figure out much faster what's going on with the trial across the board," O'Donnell points out.

By engaging with issues raised by data source expansion at the earliest opportunity, companies such as ICON can ensure that decentralized trials not only significantly enhance the patient experience but deliver more timely, comprehensive insights to optimize study outcomes and, ultimately, product value. In a pharmaceutical market where data increasingly are the product, getting data management right from the start is a crucial part of the value equation.

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For more information, please visit: ICONplc.com/decentralised