opentext™

IN ASSOCIATION WITH:

PROVENTA INTERNATIONAL

WHITE PAPER

Solving the challenges of data in clinical trial supply chains for rare diseases

Introduction

Introduction: the rare disease clinical trial landscape

Rare diseases currently affect more than 30 million people in the EU[1], around 30 million people in America,[2] and a staggering 258 million people in Asia.[3] Shockingly, of the more than 7,000 rare diseases known about globally,[4] for 95 per cent of them there exists no treatment of any kind.[5]

Developments such as the Orphan Drug Act of 1983 in the US have encouraged pharmaceutical manufacturers to focus on developing treatments for rare diseases – but the nature of those diseases has several impacts on the clinical trial supply chain. Firstly, clinical trials are much smaller for rare disease therapies, since they affect a much smaller portion of the population. In part because of this, clinical trials for rare diseases are becoming more geographically dispersed as manufacturers attempt to boost the number of participants in the study. Both facts increase cost and complexity in the supply chain, as smaller batches of medicines are created and shipped to diverse locations around the globe.

These factors are present alongside a wider set of trends impacting the clinical trial space, including:

- A greater focus on cost-efficiency in clinical trials. Deloitte research indicates that the cost of bringing a drug to market increased from $1.19bn to $2.17bn between 2010 and 2018.[6]
- A rise in complexity as manufacturers respond to a desire from regulatory authorities to see test data from populations all over the world.
- An increase in direct-to-patient (DTP) trials, also known as siteless trials.
- A drive to increase the traceability of medicines, partly due to legislation and partly due to a desire for increased efficiency and patient safety.[7]

Put together, these factors ultimately translate into tighter margins, increased complexity, and less room for error when conducting clinical trials for rare disease therapies. In turn, that means the supply chain for those trials must operate at peak efficiency to ensure that medicines can be brought to market successfully, and ultimately save patient lives.

In this paper, we're taking a look at the challenges data can pose in the clinical trial supply chain – and what organizations can do to help data work for them, rather than against them, to continue developing life-saving therapies profitably.

Contents

EDITOR:
Joshua Neil, Proventa International

WRITER:
Jonathan Oxtoby, Proventa International

CONTRIBUTORS:
Ferdi Steinmann, *Global Industry Strategist for Life Sciences*, OpenText
Arul Joseph, *Senior Director, CMC Pharmaceutical Development and Clinical Supply Chain*, Avanir

Why focus on data?

We acknowledge that there are plenty of other options when it comes to improving supply chain in the clinical trial space. IoT systems and smart labelling are among some of the innovations that aim to simplify and add intelligence to the supply chain.

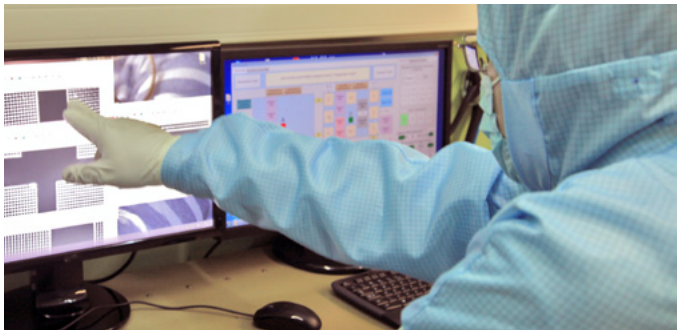
In our view, data is at the heart of the most fundamental challenges in clinical trials today. For instance: increasingly, data for clinical trials is being uploaded directly to an electronic data capture (EDC) system via a tablet or smartphone, instead of being handwritten and transcribed later. This is obviously an improvement – but if that data isn't then stored correctly, made available to researchers at the right time, or combined with other data points (such as those gathered from wearable devices worn by patients in the trial), its usefulness – and therefore the return on investment in EDC – is limited.

Central to our discussion is the idea of turning data into *insight*. This means analyzing, presenting, and combining datasets in new ways to derive meaningful and actionable intelligence from them. While there are many point solutions that assist in the gathering of *data*, unless that data can be analyzed to generate true *insight*, manufacturers will never be able to increase trial success and bring new medicines to market faster.

> *"Central to our discussion is the idea of turning data into insight. This means analyzing, presenting, and combining datasets in new ways to derive meaningful and actionable intelligence from them. "*

Challenge 1: Data interoperability

It's somewhat of an oddity that there exists no standard format for the gathering of clinical trial data. While the International Council on Harmonization has put some standards in place, these are only recommendations and not currently mandatory. Everyone from contract research organizations (CROs), to clinicians, to contract manufacturing organizations (CMOs), to sponsors, is free to collect data in whatever form they wish – with the result that data can exist in a variety of different layouts, formats, and file types across the supply chain. In fact, this challenge has been acknowledged as far back as 2016[8], and since then attempts have been made to address the challenge of interoperability – including legislation that demands interoperability such as the 21st Century Cures Act.[9] However, most of this seems to focus on the connecting of trial data – linking electronic health records (EHRs) with EDC systems, for instance – and not on the aggregation of logistical data such as shipping records, stock levels, and so forth.



This is further complicated by the lingering presence of analogue data in the supply chain. Often clinician notes are handwritten, to be typed up later, and it's been estimated that 75 per cent of medical communications in the US are sent via fax.[10] The process obviously increases the risk of errors being introduced, or data not being digitized at all and being left out of any final analysis.

The rationale for this is that it's often easier to gather data by hand when interviewing patients (or if patients are recording their own data in DTP trials); concerns were even raised as far back as 2016 that electronic note-taking would lead to less expressive notes and encourage long and incomprehensible note-taking.

However, a study published in *The Journal of the American Medical Informatics Association* revealed that electronic note taking not only improved the quality of those notes, but it also improved the length, too.[11] Despite this, the presence of handwritten notes remains.

The final consequence of the challenges posed by data interoperability, of course, is that it can be harder for organizations to gather evidence from their trial for submission, or to demonstrate regulatory compliance, simply because the data they need is hidden in an unfamiliar format, or in a handwritten document. In turn, this slows down the trial process and could even threaten the outcome of the submission, increasing the cost and time of bringing a new therapy to market.

Systems to find order in the chaos

Obviously, the drive for interoperability is in part because it's not realistic to impose a single method of recording and sharing data on the entire supply chain. Instead, what's needed is a way to pick the relevant data out of a variety of different document formats and present it to users in a way they can understand. This enables CMOs, CROs, clinicians and other parties to continue to work in the way that's most comfortable for them, while removing the complexity of managing a wealth of different document types and formats.

Additionally, technology such as optical character recognition (OCR) is important for organizations to leverage - or, to be more precise, 'intelligent' OCR. Standard OCR will help organizations to convert handwritten notes and printed documents into a digital and editable format. Intelligent OCR extracts information beyond just text, regardless of the channel of communication used, whether paper, electronic or remote data. It also adds document metadata and types to a file, so that the information within the document isn't simply recorded and stored – it's used to generate insight.

It's also essential that whatever solution organizations look at connects both seamlessly and securely with their interactive response technology (IRT) solution, rather than replacing it.

What is OCR?

Optical Character Recognition (OCR), which scans typed or handwritten documents and transforms them into editable text on a computer, is one of three types of character recognition technology that exists in the market today. The other three options are Optical Mark Recognition, which reads 'mark sense' fields such as check boxes; Intelligent Character Recognition, which text written by human hand; and Intelligent Document Recognition, which provides the following capabilities: classification, extraction, and release that transform unstructured information into a driving force that stimulate improved processes and better insight.

In the clinical trial supply chain, OCR has great potential for digitizing printed, faxed or hand-written notes that would otherwise need to be typed up by hand. Going a step further, intelligent OCR can analyze the contents of those notes alongside data from across the supply chain to unlock new insights, increase patient safety, and reduce cycle times.

> *"Data flows along the supply chain in a very linear fashion now, with each party working like a link in a chain. Each of those links can see the one next to it – but getting a view of the entire supply chain is very hard..."*

Challenge 2: Overcoming data silos

Across the clinical trial supply chain, data exists in several locations:

- With the trial sponsor
- With contract development and manufacturing organizations (CDMOs)
- With the third-party logistics (3PL) organization handling delivery of medicines from manufacturer to sites or patients
- On-site, if the trial is site-based
- With the clinicians conducting the trial
- With the patient, if they are using wearable devices to track their progress through the study.

Currently, very limited amounts of data flow between these different parties – and when it does, it's often in different formats that don't easily translate between organizations.

This is why, often, sponsors have no to limited visibility to what happens to the medicines between leaving their factory and arriving with the patient. Avanir Pharmaceuticals, says:

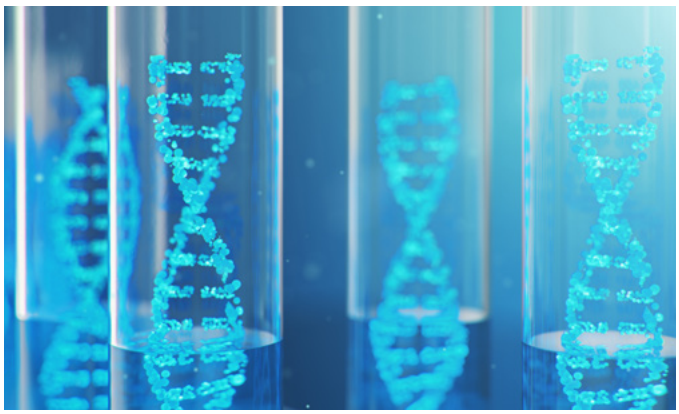
"Data flows along the supply chain in a very linear fashion now, with each party working like a link in a chain. Each of those links can see the one next to it – but getting a view of the entire supply chain is very hard. It can make activities like forecasting quantities of an investigative medical product (IMP), in the right doses, and with the right labelling for a specific country, very hard.

And in a rare disease setting, the challenge is increased as you have smaller trial sizes, and often greater geographic dispersion."

Taking one step back, data silos even exist between different business units within pharmaceutical companies, which can limit opportunities for breakthrough innovations and new drug discovery. And when time comes to prepare documentation for submission to regulatory bodies, if data isn't readily available – or is out of date – then submission is delayed or even jeopardized.

The reasons for these silos are many. Sometimes it's due to an organization's inability to get a clear view of all its data and where it is stored (especially true if they have engaged a point solution such as sensors without a plan to manage the data those sensors generate).[14] Sometimes it may be due to legacy technology that doesn't make sharing data across departments or organizations easy.[15] In the context of clinical trials for rare diseases, cross-border data sharing presents challenges as trials often span multiple countries, creating concerns around how data is handled as it crosses borders.[16] It can even be down to a historical mindset across organizations that dictates data should not be shared, so as not to lose competitive advantage.[17]

Whatever the reason, this disconnected approach increases the risk of delays in the delivery of drugs to patients – or an increased cost as you manufacture more drugs to overcome supply chain challenges – and even increases the risk of adverse events if incidents like temperature excursions aren't reported in a timely manner.



Creating a single source of truth

To overcome the challenges of data silos, organizations should invest in systems that are capable of identifying, orchestrating, and disseminating data relevant to each stakeholder, from a wide variety of sources, without the need for human intervention. Those sources should include in-house file repositories, email records, scanned documents, even handwritten notes and data from medical devices. Modern document management systems should be able to identify important information in these documents, such as shipping dates and batch numbers, presenting them in a way that's easy for users to understand.

On top of this, organizations should investigate leveraging technologies such as artificial intelligence (AI) and machine learning (ML) to uncover insights without the need for humans to analyze every scrap of data they collect. For instance, Berg Health is using AI to interrogate data and find new links between chemicals in our bodies to tackle rare and serious diseases, including Parkinson's Disease.[18]

What are AI and ML?

Artificial intelligence the phenomenon where a machine is capable of perceiving its environment and responding to that environment in order to successfully achieve a goal.[19] As opposed to machines that simply carry out pre-defined tasks with no regard to the environment around then, artificial intelligence is capable of learning and adapting how it operates. For instance, self-driving cars use artificial intelligence to adapt to the conditions on the road around them, rather than simply driving from A to B with no regard for traffic, stop signs, and so on.

Machine learning is often described as a subset of AI, specifically concerned with making predictions or decisions based on existing data. A common application of this is in email spam filters, which are programmed over time to learn what emails should be filtered out, and which should be presented to the user.[20]

These technologies combined have great potential in the clinical trial space to analyze vast quantities of data and draw meaningful conclusions from it. This includes identifying promising new therapies and drugs for consideration, but also analysis of manufacturing data to suggest quantities of raw materials needed to meet supply and demand, making continuous manufacturing in the clinical trial space feasible.

> *"Artificial intelligence the phenomenon where a machine is capable of perceiving its environment and responding to that environment in order to successfully achieve a goal. "*

Challenge 3: Wrangling IoT data

Increasingly, organizations are integrating the internet of things (IoT) into their clinical trials. There are two main avenues where IoT can add value: firstly, IoT can be used to aid in the real-time tracking and monitoring of medicines, which is important for adherence to legislation such as the Drug Supply Chain Security Act (DSCSA) in the US or the Falsified Medicines Directive (FMD) in the EU. Smart sensors attached to medicine lots can track attributes such as temperature, humidity, and location, so organizations can tell in an instant whether a medicine has been damaged, and where it is. This technology is still in the pilot stage, but promising pilots include UPS Premier, which provides instant tracking of medicine shipments throughout transit, rather than at key points as is currently the case.[21] Deloitte also describes some exciting possibilities of sensor-based shipment quality and adherence tracking, and of using blockchain to create a tamper-proof track and trace system for medicines.

Secondly, IoT devices could be used to improve the patient experience during a trial, particularly in DTP trials. Sensors can track and transmit key data on patients directly to the clinician without the need to visit the doctor's office, and even remind patients to take medications at the appropriate time. Research from Valencell found that in 2019, 1,400 clinical trials in the US used wearable devices to gather data; that data included heart rate, sleep, glucose monitoring, sweat analysis, even UV tracking.[22] Excitingly, these devices mean that DTP trial data can also count as 'real-world' data, which is an important factor in getting approved medicines moved up to higher tiers of medical insurance cover.

These innovations are essential to creating end-to-end visibility and traceability in the clinical trial supply chain – but with each device generating and transmitting large quantities of data, it's important that organizations are in a position to collect, interpret and govern that data alongside everything else they have to collect and process.

What is IoT?

The Internet of things is a term used to reference an ecosystem of connected devices, all generating and transmitting data without the need for human or machine intervention. IoT devices include smart meters in homes, wearable technology such as fitness watches, and smart sensors that can monitor and detect a range of phenomena including humidity, heat, and impacts.[23]

The value of these devices is that they are constantly gathering and transmitting data, which in turn can be analyzed to generate new insights in various fields. Some fitness trackers, for instance, can be used to track sleep simply by being worn overnight. As we describe in this paper, IoT devices have great potential to aid in the movement of medicines through the clinical trial supply chain, and to help with the gathering of data – especially in DTP trials. In fact, the value of IoT to the medical sector is such that a sub-category of IoT devices has arisen: **the Internet of medical things, or IoMT.**

Look for information management systems that go beyond conventional documents

To ensure that the data gathered by IoT devices is transformed into insight, it needs to be stored and interpreted alongside all other study data that organizations collect. Organizations should look for information management systems that can accept IoT data inputs from any kind of device – from humidity sensors to heartbeat monitors – and that can intelligently link that data to patient records, lot numbers, and so forth. By combining timestamped IoT data with things like shipping logs, organizations can create a fully transparent and detailed picture of how their medicines move from factory to patient, and quickly identify medicines that have been damaged before they are used in a trial.

It's also essential that whatever solution organizations look at, it interacts smoothly with their interactive response technology (IRT) solution, rather than replacing it.

A new world: lifesaving drugs brought to market quickly and profitably

If organizations can solve the three broad challenges that we've outlined in this paper – data silos, compatibility of data across the clinical trial supply chain, and the successful integration of IoT data – then they can unlock a whole raft of possibilities in their clinical trials.

With data flowing end to end through the entire supply chain, accessible to all, organizations can adopt a proactive posture in various areas.

For instance, with accurate data on the consumption and transit of medicines, production of new medicines can be timed to reduce waste (and therefore cost).

Risks such as temperature excursions can be identified and acted on far sooner, increasing accountability across the supply chain and patient safety. Patient safety can also be improved by streamlining the reporting of, and response to, adverse events. And crucially, with data being gathered and analyzed in real time, cycle times can be greatly reduced for trial submission data.

From a management perspective, correctly leveraging data will simplify regulatory compliance and the submission process. By smartly identifying and surfacing all the relevant documents to users engaged in each task, it's much easier to demonstrate compliance with regulations in different countries, making multinational trials simpler to conduct. The same process makes it easier to complete submissions by ensuring that project teams have all the necessary data on hand – even if that data changes while writing the submission.

> *"If organizations can solve the three broad challenges that we've outlined in this paper – data silos, compatibility of data across the clinical trial supply chain, and the successful integration of IoT data – then they can unlock a whole raft of possibilities in their clinical trials. "*

Perhaps most exciting is the ability to gather real-world data during your trial. Currently, once a medicine has been approved for use, many insurers require more data of the medicine's efficacy and safety in real-world environments before they will move it to a higher tier of product. But if organizations can correctly aggregate their data from DTP trials, they can demonstrate real-world success of their medicines much faster, moving their medicines up the tier system faster.

With the right data management infrastructure in place, organizations will also find themselves in a good position to take advantage of future developments with minimal adjustments to their existing systems and processes. Advances in smart labelling, new methods of tracking medicines or patients during a study, even AI that enables predictive manufacturing of medicines during a trial; as long as the system an organization uses is capable of receiving, interpreting, storing and presenting any data format, that organization will always be able to integrate new point solutions into their processes.

Of course, these developments all have significant business benefits. More efficient production cycles and reduced waste all reduce the cost of clinical trials and have a positive impact on cycle times. Improved patient safety obviously exposes organizations to reduced risk, and the improved ability to analyze data and complete the paperwork involved in running a clinical trial all help reduce cycle times, and the cost of bringing a new drug to market.

Ultimately, if organizations across the clinical trial supply chain invest in systems that help them manage data more effectively, they will be able to bring new medicines to market faster, and with less cost. This makes it increasingly feasible for organizations to create new therapies for rare diseases, helping address one of the great unmet needs in modern medicine.

Embrace Digital Transformation with OpenText

The life sciences industry is under huge pressure to bring safe, effective products to market quickly at a lower cost while satisfying rapidly evolving regulatory requirements – especially in the field of rare diseases, where there is a huge unmet medical need. In turn, this is bringing a laser-like focus to bear on the way organizations conduct their clinical trials. Technology will play a crucial role in helping life science organizations connect manufacturing, logistical, clinical, and patient data to transform clinical trial supply chain and deliver value for life sciences organizations.

However, current legacy systems and ad hoc processes can no longer cope with the sheer volume of patient data. To thrive in this changing world, pharmaceutical, biotech, and medical devices companies need to investigate technology solutions that:

Pharmaceutical, biotech, and medical device companies trust OpenText to help them meet information management challenges by enabling any-to-any integrations, providing an intelligent core to a broad solution portfolio, and delivering flexible paths to the cloud.

- **Enable any-to-any integrations**
  Integrate, manage, and securely exchange data across people, systems, and things
- **Provide a broad solution portfolio**
  Single, authoritative source of regulated content
- **Deliver flexible paths to cloud**
  Freedom of choice with cloud-native software that can run anywhere

For the top 20 life sciences organizations, OpenText is that partner. Our solutions, fuelled with embedded AI technology, enable organizations to move from systems of records, to systems of engagement and beyond to systems of intelligence. These systems help speed study start-ups, minimize compliance risk, boost productivity, simplify integration, and much more.

Ferdi Steinmann

is the Global Industry Strategist for Life Sciences at OpenText, with over two decades of experience in the healthcare, life sciences, and pharmaceutical industries. He has tremendous insight into the way technology helps companies succeed.

Email: fsteinmann@opentext.com
LinkedIn: www.linkedin.com/in/fcsteinmann
Twitter: @OpentextFerdi

For more information about OpenText (NASDAQ: OTEX, TSX: OTEX) visit: opentext.com

Contact us to learn more about how OpenText for Life Sciences can help you transform your organizational needs and opportunities.