Preventing costly delays in clinical trials via real-time shipment tracking

With 80% of clinical trials delayed by at least one month, optimizing the timeline of a clinical trial is a complex challenge, regardless of scale. Health outcomes for patients waiting for new treatments are at stake, as well as millions of dollars in lost days of market exclusivity for pharmaceutical companies. Real-time monitoring of investigational medicinal products (IMP shipments) is a vital new technology that helps solve this challenge, helping to ensure that appropriate participant safety and efficacy data is generated while minimizing time to market. Put bluntly, real-time shipment tracking can save lives, time, and money, and reduce waste.

This presents an exciting opportunity for pharmaceutical companies under growing pressure to gain marketing authorizations to use innovative technologies to deliver new drug therapies to patients sooner, as well as ensure return on investment. Pharma and biotech companies today can use real-time visibility of clinical supplies to investigational sites and, subsequently, increase workflow automation to avoid many of the delays in the IMP supply chain that threaten to slow down or even derail clinical trial planning.

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Clinical supply chain challenges

High throughput screening of millions of potential new drug candidates, enhanced with AI technology, aims to reduce the time to the first human studies. Scaling up to global phase III studies at hundreds of thousands of clinical sites worldwide, each with unique challenges, requires multi-billion-dollar investments. In this heavily regulated sector, where big pharma and biotechs are left with only a handful of new drug approvals each year, participant safety is the top priority, but return on investment is vital too.

Clinical trial recruitment and retention is the main reason so many clinical trials face delays. Without full end-to-end visibility on IMP availability and quality status, study managers can't plan participant site visits in advance with certainty, making it difficult to ensure recruitment targets are met, to ensure protocol compliance is achieved, and to minimize dropout rates.

Another challenge is the actual or assumed sensitivity of IMPs. Until robust stability data is generated to establish the stability budget, IMPs are often shipped in over-engineered packaging at narrower (more conservative) temperature ranges. Combined with smaller batch manufacturing and randomization packaging, which increases the impact when a package is damaged, there's a costly knock-on effect to clinical study supplies and timelines. This impact is further compounded by the growth in IMPs that are more sensitive to the environment, such as for new cell and gene therapies.

"Bringing much needed new drugs to market is a long-term and significant investment for pharma and biotech, and entails a complex and highly regulated process. There are countless points at which the agility, efficiency, and reliability of the supply chain will influence whether a clinical trial stays on track. Given this scale, small improvements to the supply chain quickly add up to enormous benefits."

Alison Riggott
Business Development Specialist at Controlant

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The implications of delay

Of the 80% of Phase III clinical trials that face preventable delays of at least a month, many face much longer delays and end up taking 3-6 months longer than planned.

Based on a conservative estimate of what this costs in lost days of post-launch market exclusivity, the price of one month's delay for a typical drug begins at around $18 million. For expensive drugs, 30 days could cost more than $200 million in lost revenue.

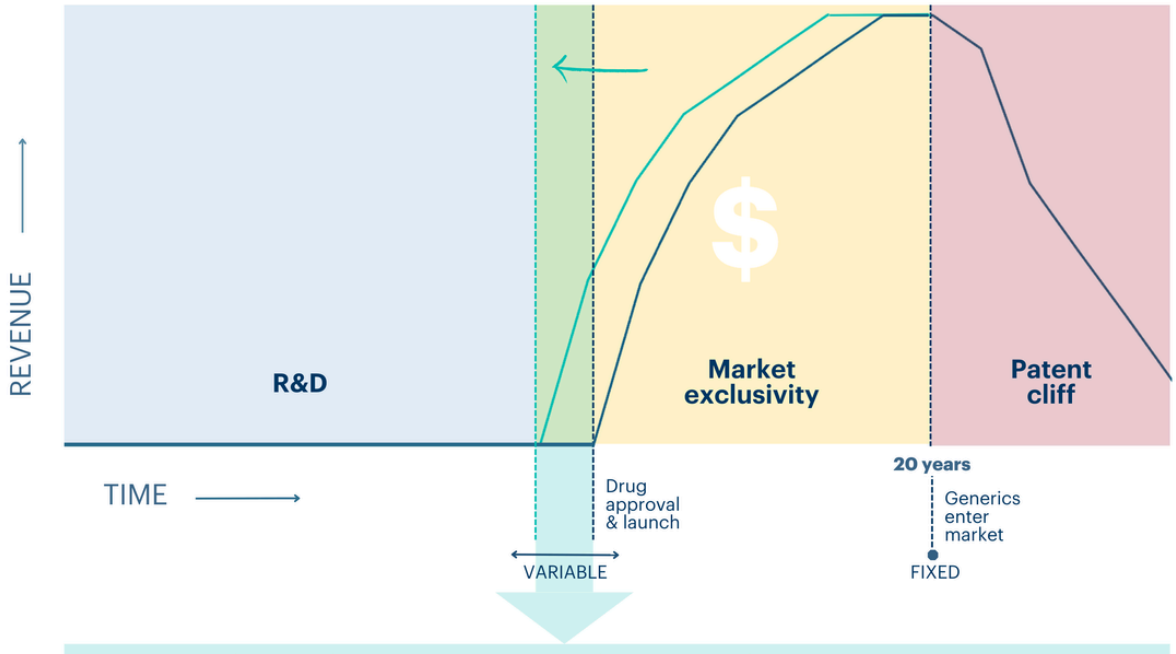
And for patients waiting for a new drug, the health costs can be life changing.

Market exclusivity is relevant because of the so-called patent cliff. Even without any delays, the whole process up to the point of a drug's marketing authorization often takes more than a decade and costs billions of dollars. It's a big investment, and the clock on the ROI starts ticking right at the start, when the pharma company first identifies the potential drug candidate. A pharma patent lasts 20 years, but when a drug takes more than 10 years to go through development and reach the market, this leaves less than 10 years of market exclusivity on the intellectual property for the pharma company to recoup and generate profit on the investment before generic equivalents reach the shelves. Every week that a new drug isn't on the shelf can add up to millions of dollars in lost sales. The point at which a pharma company loses patent protection of a drug is known as the patent cliff because of the steep dive in profits.

"The patent expiry helps ensure patients can access affordable treatments and helps drive a constant pipeline of new drugs. For pharma companies, it means time is of the essence. The combined pressure from prescribers eagerly anticipating a new drug's release and from shareholders looking for an ROI before the patent expires needs to be balanced with the time taken to generate an adequate safety profile of the therapy. This adds value to any solution that mitigates delays."

Alison Riggott
Business Development Specialist at Controlant

Impact of generics entering the market



When real-time monitoring prevents delays, it moves the line so you can get drugs to market sooner. Every week of market exclusivity can add millions of dollars in sales.

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How passive IMP shipment tracking aggravates delays

Much of what's time consuming in clinical trials cannot be shortened – we can't speed up the time required to confirm if a drug is safe and effective. But we can do a lot to shorten or eliminate some of the most common delays.

"Temperature excursions are a case in point, at the root of many delays. If you have participant visits planned for randomization or their next dose, but the IMP can't be administered because a temperature excursion is being investigated, you can't always say, 'Come back tomorrow.' The clinic may only run once a week, or the participants may not be willing or able to come back on a different day."

Alison Riggott
Business Development Specialist at Controlant

This feeds into the main cause of study delays mentioned earlier – participant recruitment and retention – but also contributes to protocol deviations with out-of-window visits, when a participant doesn't show up within the required timeframe.

Temperature excursions have a butterfly effect on clinical trials – and the consequent costs are manifold. Here are some of the areas often impacted negatively when shipment monitoring is passive:

- Time for pharma internal investigation
- Time for the quality team to prepare, communicate, and file paperwork to satisfy excursion investigations
- Time for this to be approved
- Environmental cost of discarding drugs (deemed unsafe or cleared too late to be administered)
- The need to reschedule participant visits, risking of out-of-window visits
- Cost and time of registering new participants, replacing safety follow-up of ITT population, and lost to follow-up participants
- Strain on pharma relationships with study investigators
- Protocol deviations and the cost and time of altering protocols
- Loss of access to investigational drugs
- Health cost of the delayed release

There are whole books dedicated to the challenges of patient recruitment for clinical trials, and a recent study found that one key complication is the distance participants are required to travel.

In the US, this takes an average of two hours. The longer the distance, the greater the impact of any delays that result in rescheduling. But restricting participation to people living close to a clinic is problematic as it results in data that's not representative across diverse socio-economic and ethnic groups. The study proposes that decentralized and hybrid trials go a long way towards addressing this challenge – solutions that further amplify the benefits of real-time shipment monitoring.

Irrespective of how centralized or decentralized the trial is, if a temperature excursion can be prevented or investigated before the drugs arrive at the destination, benefits include a reduction in out-of-window visits, protocol deviations, participant dropout rates, and product loss. It reduces the burden on the sites to report to pharma and manage the knock-on effects of quarantining IMP, re-scheduling clinics, and so on.

A few dropouts may not seem crucial, but this exacerbates the challenge of patient retention and recruitment, which has various consequences in addition to causing delays. When someone drops out during a trial, or is forced to switch from getting a dose on weeks 4, 8, 12 etc. to getting one on weeks 5, 8, 12, this can constitute a protocol deviation, reducing the PP (per protocol) population and contributing to the intention to treat (ITT) population, where patients are followed for safety reasons. The data needs to be statistically powered appropriately in order to compare a drug to a comparator as defined in the protocol, while exposing the proposed new medication to the minimum possible number of participants.

Furthermore, when there are participants lost to follow-up, you need to randomize more participants to reach the recruitment goal, but it's not as simple as transferring the costs associated with the original patient to the replacement one. For safety reasons, you always follow the participants who have dropped out for a pre-defined amount of time. Then there are ethical challenges too, over recruitment into the ITT population you're dosing in an unplanned manner, which can potentially compromise patient safety.

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The knock-on effect for RTSM and inventory management

When a lack of visibility places the integrity of the investigational product in doubt, it will need to be destroyed and replaced. In a blinded randomized trial comparing a new drug to an existing drug, resupplying a product is very difficult, not only because the innovative drugs are made in small batches, making it expensive, but also because the drugs are labelled with randomization codes that have been programmed within the Randomization and Trial Supply Management (RTSM) solution.

Each site has a specific allocation of blinded and coded kits, which takes extra work to re-supply. The alternative – notreplacing the missing/discarded box – is also problematic. If you're short of some product, someone needs to program this into the trial, making sure the ratio of comparator to IMP is maintained according to the randomization scheme.

That's the value real-time visibility on IMP can deliver.

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How to prevent delays with real-time IMP shipment monitoring and process automation

"When a real-time monitoring solution is integrated into the RTSM, there is an opportunity to gain value from the automation this integration unlocks. For example, if the status report is automated, the pharmacist doesn't need to go through it all and mark it off, line by line. As well as speeding up the process and reducing the load on the pharmacist, the time normally spent marking status as 'checked', 'available to use', or 'excursion detected' becomes available for more value-adding tasks."

Alison Riggott
Business Development Specialist at Controlant.

*"Electronic data loggers have been around for more than 50 years, but it's only since the advent of IoT technology that **real-time** data loggers have been developed. You need real-time monitoring devices to receive immediate alerts in case of temperature deviations and other non-compliance issues. An obvious advantage of this is that you can act pro-actively and promptly to intervene and safeguard the quality of the drug."*

Ada Pálmadóttir
VP Business Development at Controlant.

This reduces product spoilage and loss, improves sustainability, and helps keep clinical trials on track. For IMPs travelling via large challenging airports such as Mumbai, the visibility of a delay or excursion before it arrives at site (e.g. at customs clearance) gives you the best chance to intervene in time to mitigate or avoid the consequences of the disruption.

In transporting drugs for clinical trials from a primary warehouse to secondary warehouses or distribution hubs, and then to any number of clinical sites – hospitals and other points of use – real-time monitoring helps maintain the quality and safety of temperature-sensitive drugs, and helps ensure compliance with stringent industry regulations. It's one thing to transport and store products perfectly, but regulations demand that you be able to prove the data too.

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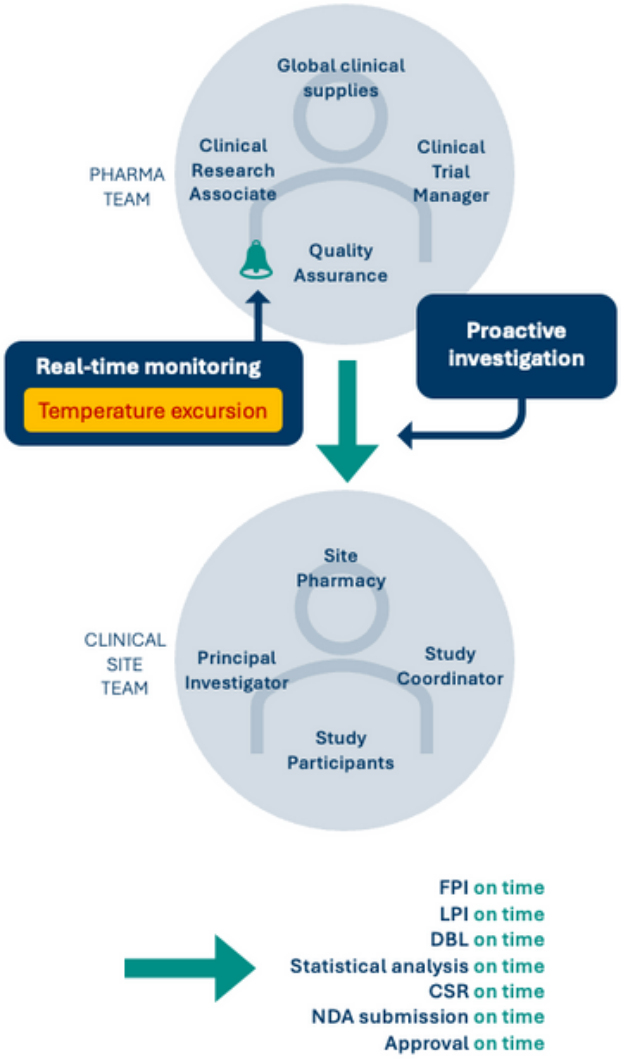
Opportunities to benefit from real-time monitoring go beyond transport, as conditions in storage at clinical sites need to keep products safe too.

From Johns Hopkins University medical storage to a small Guatemalan hospital, the expectation is that these facilities offer the same condition and thus the product delivered to participants is identical, but in reality there is a lot of variation.

Keeping clinical study timelines and budgets on track



Full visibility saves time and money

"Monitoring device technology today includes location tracking for full visibility of shipments, so manufacturers and other stakeholders in clinical management and site staff can track a product's exact location at any moment. This is a game-changer for clinical trials, as such precise tracking safeguards the quality of the data and enables you to intervene and avoid delays associated with temperature deviations – delays that can flush a whole trial down the drain."

Ada Pálmadóttir
VP Business Development at Controlant.

"Real-time visibility is a key to unlocking automation opportunities that boost efficiency – solving problems that some pharma companies may not even realize they have."

Carsten Lützhøft
CPTO at Controlant.

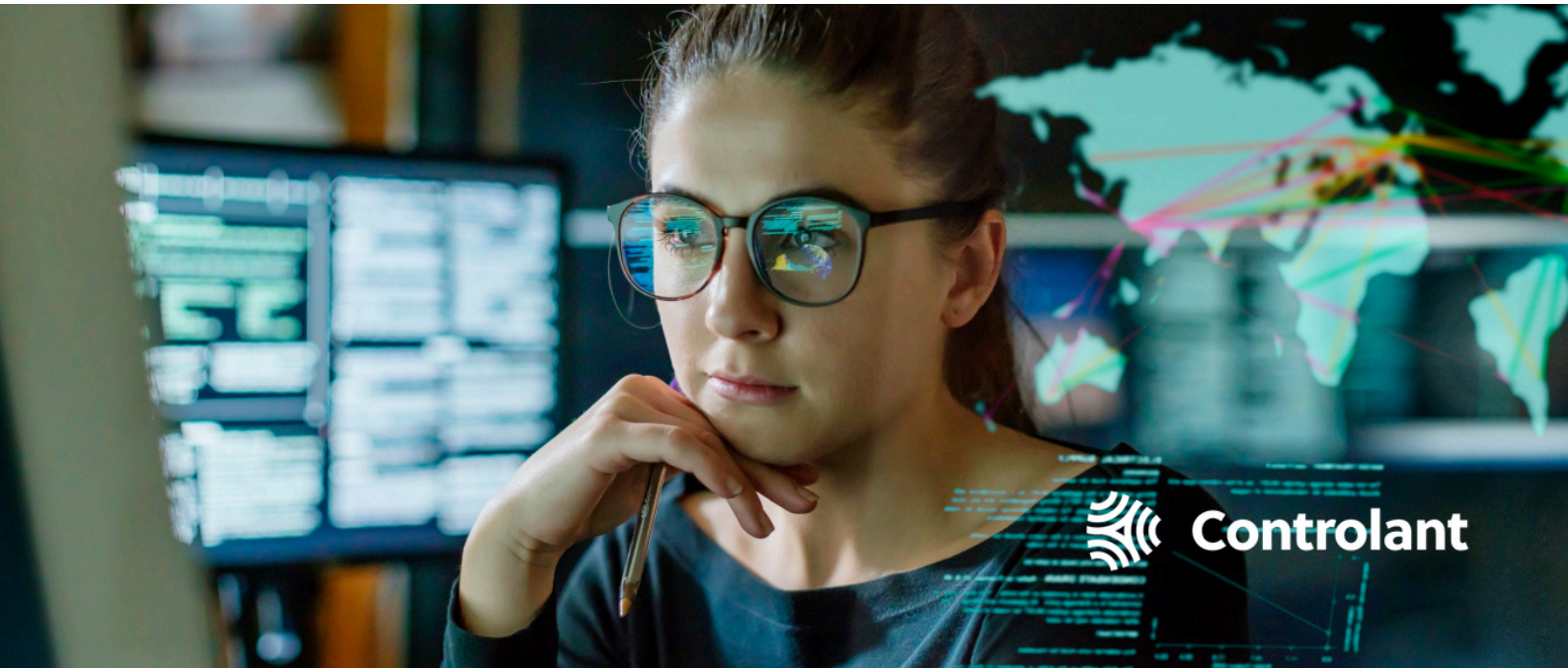
For example, automating alert notifications at clinical sites removes the burden on sites to report temperature excursions. Typically, the site isn't responsible for reporting excursions – and sometimes they don't report them all! – but in practice, the burden ends up on them.

If the pharma company can deal with the excursion en route, thanks to real-time visibility of the IMP, it's a big win for the sites and for the safety of the products. It saves on paperwork, since the delivery report can be sent automatically via email instead of needing to be printed and filed. Moreover, reports can also go to file automatically, so that the Clinical Research Associates monitoring trials have instant access to it, instead of needing to ask and wait for it, saving time and reducing both their work and the site's. With remote file reviews, they can see what's filed beforehand and spend their physical visit doing what can't be digitized, such as building their relationship with the doctors, investigators, and team.

Making life easier for site staff is a recurring pain point for customers, both in terms of finding more efficient ways of getting the data, and in terms of streamlining the filing and reporting of that data. Real-time monitoring devices contribute to operational efficiency by providing detailed insights into shipment conditions and performance, enabling you to streamline processes, communicate efficiently across large project teams, reduce delays, and enhance overall supply chain reliability.

"For logistics providers, real-time monitoring solutions make it possible for them to manage their operations proactively, anticipating and mitigating potential issues for their pharma customers before they escalate. Real-time location tracking allows logistics providers to optimize delivery routes, reducing transit times and improving delivery schedules. This enhanced efficiency translates into better service quality and customer satisfaction."

Carsten Lützhøft
CPTO at Controlant.



Improving compliance at varying degrees of digital maturity

"At clinical sites, real-time visibility makes tasks easier, processes smoother, and human error less likely. It helps the pharma company enable site staff to manage their trials more effectively."

Ada Pálmadóttir
VP Business Development at Controlant.

A common challenge for pharma companies is getting timely temperature data from the sites – data they require to satisfy regulations.

The specific pain points vary a lot depending on an organization's digital maturity. For less digitally mature companies, basic automation can have a big impact. Even today, there are sites where someone is walking around with a clipboard, checking boxes and marking on paper whether they're intact and stored at the right temperature. The risk of human error is alarming, and something as simple as replacing the clipboard with a tablet computer can already modernize the documentation and improve the reliability of the data.

Electronic site files are a pipe dream for many, but this has changed a lot in the past decade as sites become much more digitally mature. The more visibility multiple stakeholders have, the more efficient you can be. Based on current trends, electronic site files will become the norm in just a few short years.

Passive loggers are a step up from this, with someone plugging in the USB to extract the data once a shipment has arrived. A quality release isn't needed for everything, but when there's an excursion, there's a lot of communication that can't be streamlined without real-time monitoring. If there's an excursion, this contributes to the risk of delays – an email sent on a Friday afternoon might not be opened until Monday morning, or someone might attach the incorrect file etc.

There's some risk of human error when people along the chain are required to reconcile data from multiple sources, and large global studies need to account for teams being spread across time zones too.

"Real-time loggers make it possible for the pharma clinical management and quality assurance to monitor locations and temperatures via the SCM and receive automated alerts as soon as anything is amiss, which makes it much easier for the pharma company to improve their clinical supplies' efficiency and compliance. Automation of this process boosts the ROI, with clinical trial project managers no longer spending time manually managing the data."

Alison Riggott
Business Development Specialist at Controlant.

"In the most digitally mature state, data from these monitoring devices feeds into advanced AI algorithms that analyze data to identify patterns and predict disruptions. As part of an AI-enabled visibility platform, this automates decision making and enables greater proactivity – from using alternative shipping routes to notifying sites ahead of time so they can prepare for a delay. This frees up employees to focus on more value-adding tasks. As the saying goes, AI will not replace humans, but humans with AI will replace humans without AI!"

Carsten Lützhøft
CPTO at Controlant.

Integration and automation are value multipliers

Shipment monitoring solutions that integrate with existing ERP and transportation management systems will facilitate smooth data flow and operational coherence.

In a digitally mature clinical trial supply chain, real-time monitoring can enable automated product release, which significantly reduces the time needed for manual inspections and shortens the product release lead times. Likewise, for quality reports, an integrated visibility platform can save the time it takes to generate a report, and of going and looking in the files to submit a report. Instead, the report is generated automatically and can be accessed easily via the platform.

"Combined with automated and enhanced customer service, real-time monitoring also helps keep relevant stakeholders informed about shipment status, which reduces the strain on customer service operators and improves customer satisfaction."

Ada Pálmadóttir
VP Business Development at Controlant.

Like the benefits of RTSM integrations outlined earlier, eTMF integrations present opportunities to streamline the workflows of clinical teams significantly. The TMF (Trial Master File) is essential for GCP (Good Clinical Practice) compliance with regulations surrounding documentation of trial conduct and data.

The electronic TMF (eTMF) greatly streamlines the management of this documentation, with benefits that are parallel to the general benefits of supply chain automation powered by real-time visibility: automatic data collection, automatically populated report templates, remote collaboration, data security, easy tracking, and real-time transparency. By integrating eTMF with the real-time visibility platform, pharma companies can amplify these benefits.

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The urgent need to create a more sustainable future for clinical trials

The pharmaceutical industry is facing immense sustainability challenges and the urgency of solving these challenges is only going to increase. If the healthcare industry were a country, it would be the fifth largest polluter on Earth, with the pharma supply chain accounting for a hefty chunk of that pollution. New solutions and devices must be sustainable across the entire supply chain.

"When real-time monitoring devices are reusable, return logistics enable an integrated circular business model, whereby loggers can be returned from the receiving site back to the primary warehouse."

Vicki Preibisch
VP Sustainability at Controlant

As clinical trials tend to involve smaller shipments of products, often packaged in reusable boxes, with repeated trips along the same route from warehouse to site pharmacy, a circular model is more efficient, more convenient, and more sustainable than using single-use loggers.

For every dose administered during a clinical trial, for every participant, there are multiple biological samples that need to be shipped and analyzed. In future, with technology moving towards smaller devices, we will see biological samples shipments from clinical sites to central labs monitored more sustainably, potentially using the device's return trip to monitor samples, along with the return reusable packaging, further highlighting how the clinical trial supply chain lends itself to circularity.

Emissions avoided in 2023 by companies using multi-use loggers

8,203 tonnes CO2eq of avoided emissions using reusable Saga devices compared to single-use loggers*.

That's the emissions-equivalent of **driving 33.8 million km** in an average fuel-powered passenger vehicle.

*Calculations based on Controlant's Lifecycle Assessment and logistics usage data for 2023

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Coupled with an advanced platform and monitoring and response services, real-time monitoring devices can improve almost every element of the clinical supply chain from warehouse to point of use, including reverse logistics and storage on sites.

Optimizing clinical trials is fundamental to achieving the goal of bringing safe and effective medicines to more patients as quickly as possible and with as little waste as possible. It's about the people who need new medicine to live better lives. This whitepaper has explored some of the ways this can be achieved by implementing a real-time monitoring solution.

Contact us if you'd like to learn more about the benefits of real-time monitoring technology for the clinical trial supply chain.

Our experts are ready to discuss how Controlant's real-time visibility solution can be tailored to your needs to transform your clinical supply chain and accelerate study timelines to bring new treatments to patients faster and more sustainably.

Contact us

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Key recommendations

Start with low-risk high-yield improvements

The potential ROI of implementing real-time monitoring to reduce delays is your clinical trial supply chain is significant. Phase 3 can be the best place to start because that's where you have the most to gain, especially when there are many international and highly varied sites.

Ensure compliance

Not all high-tech data loggers and visibility platforms are built for pharma. Ensure your investment is pharma-validated and -verified, complies with the legal standard under 21 CFR Part 11 / EU Annex 11, and is governed by all the necessary SOPs.

Further sustainability

Make sure the real-time monitoring solution supports a circular business model with reusable monitoring devices and return logistics, combined with reusable shipping boxes, and that the solution provider has a science-based climate action plan, measures and reports transparently on its ESG data, and reports its sustainability performance through third-party assessments such as EcoVadis and CDP Climate.

Maximize integration

Clinical trials are already laden with multiple systems that don't talk to each other. A platform that integrates with your RTSM, eTMF, and other systems will have more impact, will be easier for your employees to adopt, and will make their jobs easier more quickly.

Automate workflows

Identify where automation will have the greatest impact – if your Phase 3 trials are constantly delayed by manual intervention at the point of product release, automate this process by digitizing, storing, and processing stability profiles in your visibility platform. To make life easier for pharmacists or site staff, workflow automation such as automated report management will streamline processes and reduce the manual load.

Keep it simple and holistic

Advanced services and a GxP-validated visibility platform with a user-friendly interface will help ensure you make the most of your real-time monitoring devices. Non-account holders will need access to data too, such as shipment quality information. This is a huge benefit at clinical sites, where there are high numbers of staff and often high turnover too, giving you full control of who sees your data and providing access without needing to set everyone up with their own accounts.

Let the experts support you

Effective implementation and training services, combined with ongoing support from a customer success manager, can make a big difference to the impact and long-term optimization of a monitoring solution, especially when affected users are spread across thousands of sites. For day-to-day operations, a monitoring and response service provides the expertise and responsiveness that will keep your supply chain running smoothly.

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Carsten Lützhøft

CPTO, Controlant

Carsten Lützhøft has extensive experience of process digitalization in the global manufacturing and supply chain sectors. He serves as board member and advisory board chairman in scale-up companies within the aviation and health tech industries.

Adalheidur (Ada) Pálmadóttir

VP Business Development, Controlant

Ada leads the global roll-out of Controlant's real-time supply chain visibility solutions. She is an expert in sales, operations, and marketing, specifically in the areas of product, vertical alliance sales, and partnerships related to pharmaceutical products. She is a licensed pharmacist with an MBA degree.

Vicki Preibisch

VP Sustainability, Controlant

Vicki is responsible for heading ESG and leading a team of sustainability professionals to accelerate Controlant's sustainability journey, while enabling the company's customers to deliver on their climate strategies. She is also Chair of the UN Global Compact Leadership Council for Iceland.

Alison Riggott

Business Development Specialist, Controlant

Alison has more than 20 years' experience in clinical trials operations oversight. She is a qualified pharmacist and before joining Controlant held global clinical roles within Pharma, CRO, and the medicines regulatory industry.

Contact us

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