berlinger

Case study

The value of implementing end-to-end temperature monitoring and assessment in your clinical trial supply chain

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Introduction

The main aim of sponsors when conducting a clinical trial is to deliver the Investigational Medicinal Product (IMP) to the patients in the quickest, most efficient, and safest way possible. The best approach to achieve this is to implement uninterrupted temperature monitoring in the IMP supply chain, starting from IMP packaging and including IMP storage at site. This will simplify executing processes and facilitate decision-making on whether the IMP is still fit for use and thereby secure patient safety.

Very recently, Berlinger had the opportunity to implement its SmartView end-to-end temperature monitoring system within one clinical oncology study conducted by the healthcare business of Merck KGaA, Darmstadt, Germany. Before the clinical study started, the sponsor had a manual process where the temperature measurement process was fragmented and did not allow for efficient cumulative tracking.
Simultaneously, the whole process was documented on paper basis, which is more time-consuming and prone to human error. This might cause delayed decision-making, due to the lack of online access to all necessary data along the supply chain.

Ultimately, the nature of non-digital processes could potentially lead to costly expedited shipments, delayed patient treatment, drug wastage and potential risk of compromised compliance with regulatory requirements. Berlinger understood the weaknesses of the process faced by the sponsor and engaged in a collaboration with all stakeholders involved in the study supply process to make sure that our client's QA (= Quality Assurance) department could work more efficiently. Thanks to Berlinger's open SmartView platform, it was possible to integrate the Berlinger system with the IRT platform that helped Merck KGaA, Darmstadt, Germany to gain online access to the cumulative overview of IMP temperature data during storage and transport. This allowed all stakeholders involved to maintain one platform, with one dashboard and full oversight of the complete temperature history of the IMP.

The key to success in this project was the collaboration between different stakeholders involved in the study such as the sponsor, the CDMO, the CRO, the sites, and their IRT partner. In this case study the technical background of Berlinger's SmartView end-to-end temperature monitoring and assessment solution, and the benefits of implementing it in the clinical trial for each stakeholder will be discussed. In addition, this paper outlines the lessons learned from the implementation of Berlinger SmartView solution and lastly, the outlook for the future and a sneak peak of what is to be expected next from end-to-end monitoring in the clinical trials industry.

About the trial

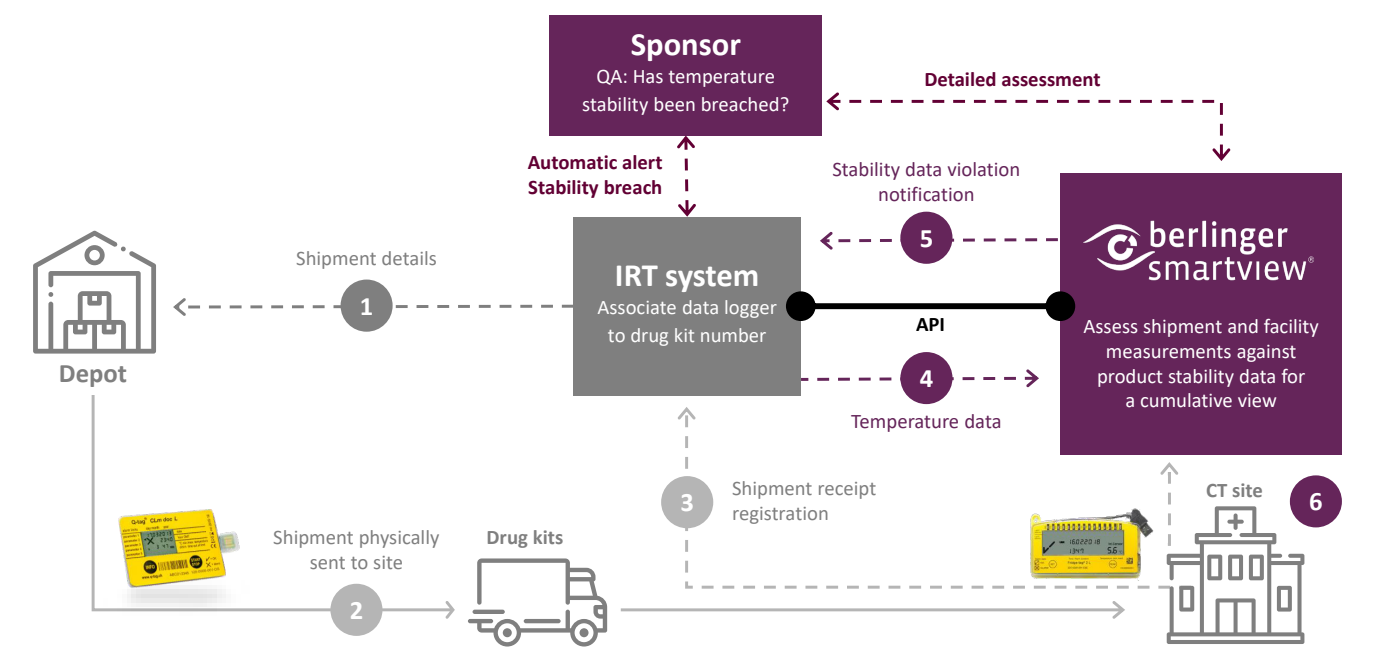
- **Trial duration:** 48 months
- **Number of IMPs:** 4
- **Estimated enrollement:** 252 participants
- **Number of countries:** 13
- **Number of sites:** 114
- **Estimated number of shipments:** 2520
- **Number of depots:** 4
- **IMP temperature storage requirements:**
  - 2-8 °C
  - -20 °C
- **Berlinger solutions used in the study:**
  - SmartView platform
  - Q-tag CLm doc L
  - Q-tag CLm doc Ice
  - Fridge-tag 2L
  - Fridge-tag 3


Status: Analysis

Connecting the dots

When implemented correctly in the study, the process of temperature monitoring can become seamless and create an effortless stream of data between the stakeholders involved. For a better understanding of how implementation works, the following diagram shows how the IRT and the Berlinger SmartView communicate with each other to render a cumulative overview of the

required storage conditions established for the shipment (4). In case of a temperature excursion occurring, a notification is sent to the IRT system, which puts the IMP in quarantine, and additionally informs the IRT of the stability breach (5). This is when the sponsor's QA team steps in to determine if it is still in a fit state to be administered to the patients or not.



temperature profile from depot to site. CDMO software integration with the IRT system is also an important factor of success. **The essential part of the solution is the connection of the IRT with SmartView via the Application Programming Interface (API).**

Initially the shipment details are provided to the CDMO (1). Then the process continues when the CDMO adds a Berlinger shipment logger (in this case a CLm Doc L) to the Clinical Trial Supplies and the IMP is shipped. (2) At the next step, upon arrival at the clinical trial site, the shipment receipt information is sent to the IRT system (3). Before implementation, this task was performed manually by the site staff, which was time-consuming and prone to human error. Berlinger's shipment logger is connected to the computer and automatically creates a PDF report, which is then uploaded to the IRT system. This allows the temperature data to be shared with the Berlinger SmartView solution platform that compares it to the

The same process is performed in the case of site temperature monitoring, where the team onsite uploads the reports on a predetermined basis or in case of the real-time data transfer, everything is done automatically, and no additional effort is needed from the site's staff (6).

The described process shows that even though temperature monitoring can be rather complex, given the complexity of the supply chain, the implementation of end-to-end temperature monitoring simplifies this process. Thanks to the user-friendliness of Berlinger's SmartView system and its integration with the IRT platform, it can become automatized and remove manual tasks which were previously required within the process. This is especially the case since the IRT platform remains the front face for all the study stakeholders that are now equipped with additional information on temperature monitoring of the entire cold chain journey of the IMP.

The advantages for each stakeholder

During this project, the Berlinger team was able to learn more about how the implementation of the system affected each one of the stakeholders participating in the study and how they were able to benefit from it. The key factor of success is that the IRT system remains the front-face so system implementation in the existing processes remains straightforward for all stakeholders involved.

Sponsor
By implementing the SmartView open platform for end-to-end monitoring, the QA department of the sponsor can oversee the complete journey of every single IMP 24/7. This allows the whole team an easy, fast, and reliable temperature assessment process and is in line with the sponsor's ambition to drive digitalization. It also reduces the risk of human error and improves a collective oversight of data, which can avoid expensive expedited shipments, unnecessary IMP wastage or even rescheduling patient's visits.

CRO/Site
The solution implemented with Berlinger's temperature data loggers and automation of the process enables the sites' staff to spend less time on temperature monitoring tasks, which then ultimately reduces human errors.
In cases where the real-time data transfer has been implemented, and the process has been automatized, the workload from the sites' staff is minimized to manual data upload only in case of temperature excursions or lack of data connection, in which case the temperature is uploaded once a month. Obtaining higher efficiency and accuracy on the part of site staff by reducing the burden of process work is an advantage the sponsor can seek by implementing the solution in their trial.

CDMO
Access to a complete overview of an IMP's journey is crucial during the clinical study, especially when the drug kit is being shipped to various depots before it finally reaches the designated site and ultimately is administered to the patient. The implementation of the system and complete overview of data enables streamlining of the monitoring processes. Lastly, the training of the whole system and the loggers took no longer than 30 minutes on the CDMO's side thus ensuring quick system implementation and in turn, rapid resupply in case of excursions in the transportation of the IMP.

> "Partnering with Berlinger on our fully automated cumulative temperature management solution has been great. They share our passion for innovation, quality and customer focus. Together, we are changing the way temperature management is carried out in clinical trials from a manual, paper-based and cumbersome process to an automated and instant excursion review and decision with full cumulative end-to-end visibility for each drug kit at your fingertips."

Stefan Dürr, Senior Director, Client Delivery at Cenduit IRT

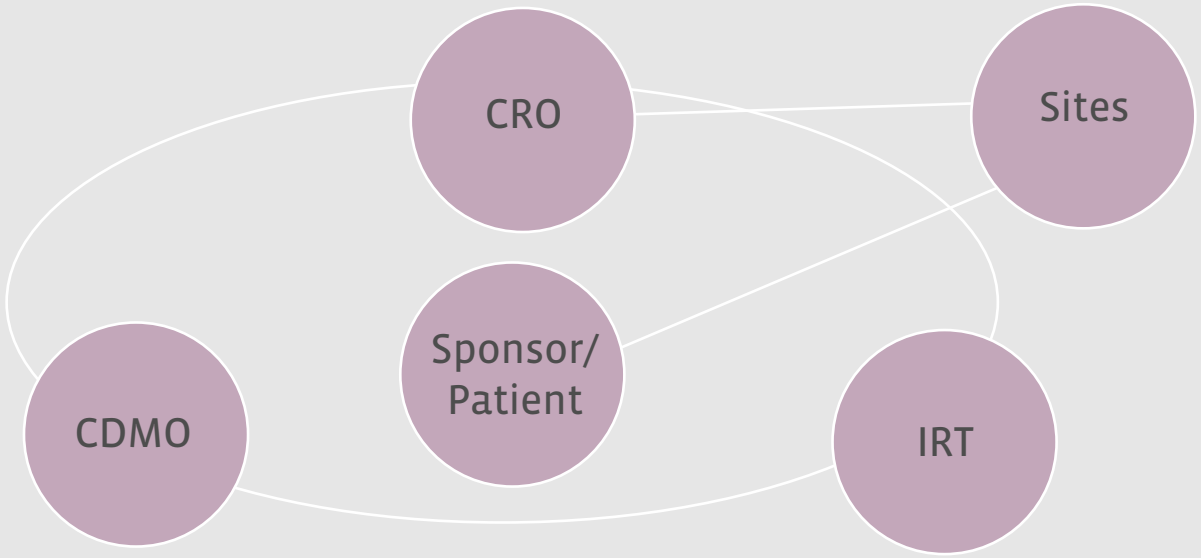
"The benefits of using integrated end-to-end temperature monitoring in your clinical study is clear to see, particularly from a distribution perspective. The streamlined monitoring of temperatures during shipments to clinical sites will significantly reduce time spent by all parties in managing this process. The SmartView dashboard is incredibly user-friendly and provides great oversight on the temperature status of shipments across the board."

Leigh McGonigle, Clinical Supply Manager at Catalent

The relationship between the stakeholders

Each of the above-mentioned parties played a crucial role in implementing this project of end-to-end monitoring and assessment within the clinical study.

Individual stakeholder processes then had to be adjusted so as to synergize with the group and to function as an integrated team to achieve the final goal of the



It was important to ensure that while working on the implementation of the system that the appropriate team members on the stakeholders' side were involved and that they had the knowledge necessary to move this project forward.

Additionally, the team had to ensure that there was a clear distribution of responsibilities between each of the stakeholders, which essentially converted into an establishment of a RACI matrix with the clear division of deliverables assigned to each party. Since the stakeholders had already established their internal processes which allowed them to create an overview of temperature data monitoring within their scope, those needed to be adjusted to implement Berlinger's SmartView solution platform into the picture.

safety and efficiency of this clinical study. This task was performed by establishing a clear communication between the parties involved, which ultimately turned out to be an essential ingredient of making this project successful.

When reflecting on collaboration between the stakeholders, Leigh McGonigle from Catalent, states the following: **"From an operational perspective, implementation for our pilot study was at times challenging as we all entered novel territories and adopted new processes across several key stakeholders. Collaboration is key to success however, and continuous communication with key technical experts to ensure the integration between CDMO, IRT & Berlinger is crucial to identify and resolve issues as they arise."**

The results

This pilot with the healthcare business of Merck KGaA, Darmstadt, Germany has shown the various benefits of end-to-end temperature monitoring, not only for the sponsor but also for all of the other stakeholders involved in this study.

1 **Expected saving in IMP wastage and minimization of expedited shipments**

2 **Compliance with increased regulatory requirements**

3 **Minimization of human prone errors**

4 **Time and workload saving on site-performed tasks**

5 **Instant temperature excursion assessment**

Where are we going next?

“End to end temperature monitoring and assessment - a manual process goes digital, our step into the future.

The implementation of the new processes challenged us more than expected during the set up but also during the implementation in the first trial. Dealing with multiple stakeholders from different companies and aligning their diverse expectations was one of the biggest hurdles to be taken. Furthermore, the transfer of the defined process into a real trial was another big hurdle, but we made it! Our driver was our belief in the benefits of the digital transformation such as enhanced data collection, increased data-driven insights and better site personal experience.

All benefits result in a robust supply chain for our IMPs which our patients in particular will benefit from.

Silke Leiser, Global Clinical Trial Supply Director at Merck Healthcare KGaA

As laid out in this case study, end-to-end monitoring and assessment helps to create complete oversight, better compliance, improve process efficiency, faster decision making and ultimately helps to improve patient safety.

Therefore, the next step is to deploy the digital process to all studies performed by the healthcare business of Merck KGaA, Darmstadt, Germany with the aim of positioning them as the sponsor of choice.

We are just at the beginning of the trial, more information and data on the study will be released in the near future.

Berlinger’s next-generation outlook
In addition to these steps, next steps from a technological perspective can be made. Berlinger’s state-of-the-art **SmartSystem - the first certified climate neutral product in condition monitoring -** employs the latest wireless technology to support real-time monitoring. This allows for real-time oversight and decision making and a further reduction in workload for e.g., site staff as no human intervention is required for daily operation of the monitors.

Berlinger’s modular real-time technology allows users to use real-time technology with all its benefits in a cost-efficient manner through intercommunication of all devices involved in a particular study. SmartSystem lets the end-user go beyond temperature monitoring as it enables:

- GPS tracking, so the user not only knows when an excursion took place, but also where an excursion took place.
- Humidity to track the relative humidity profile of the drug-kit.
- Light to track whether a package has been opened during the clinical supply chain.
- Shock to detect whether a drug kit has been dropped.

All-in-all, SmartSystem helps the end user to track where the drug kits are and their condition in real-time, combining sustainable choices with significant cost reductions through modular real-time.

Looking for a way to implement end-to-end temperature monitoring in your clinical trial?

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