The Evolution of Environmental Monitoring

Global clinical trials require multifaceted logistical support in pharmaceutical and biological sample transportation. Choosing one of the various technologies on offer that best fits a particular process can make clinical logistics safer and more efficient

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Clinical trials are a complex undertaking and a huge investment for the sponsor, taking a significant amount of time to complete and to produce a marketable drug. Added complexity comes from the inherently global nature of recent clinical trials which are spreading operations over multiple nations, sites, and premises. Ensuring sufficient enrolment numbers and monitoring activities on multiple sites and suchlike justifiably take up a major portion of sponsor and investigator focus.

A Complicated Process

With the vast amount of analytical activities in a clinical study, it is easy to forget that even in national – and more so, in international studies – logistics complexity is a major concern. However, while logistics is a support function for the overall trial operation, it also needs planning to function efficiently.

In a drug trial, ensuring that the investigational medicinal products (IMPs) reach the site in good condition and that samples travel from collection points to laboratories in correct environments is paramount. With lab specialisation requiring long transportation distances and the parallel supply chains of international, regional, and local hubs often working without visibility to each other, guaranteeing the integrity of the supply is not always easy.

An additional challenge is presented by the increasing interest in home trials and direct-to-patient logistics. These may help with retaining volunteers for the duration of the study by making it easier for them to take part. However, they

also raise questions about the handling of last mile logistics, a fairly recent development in a clinical trial context.

Developing Logistics

In this kind of international clinical study, the investigator is likely to be working with multiple logistics operators. This can create challenges for the integrity of IMPs and samples, as different logistics operators have varied ways of handling the control and monitoring of environmental conditions in their storage and transportation, not to mention handover protocols. It is also a situation which is likely to cause functional siloes of data.

Even though the logistics manager should have visibility to the diverse means of environmental data gathering and control of their subcontractors, all that data rarely transfers to a central base for overall analysis. This leaves any possible excursions as individual problems instead of creating a picture of the overall logistics network function, which could work as a model and dataset for improvement.

The counterpoint to this is that, with logistics data capture moving constantly towards more electronic means, it should not be a difficult undertaking to compile all the information into a map of actual process for development purposes. One of the reasons why this is not a common procedure is the current diversity of technologies meant for handling environmental data monitoring. Another is the insufficient engagement of stakeholders to end-to-end logistics visibility.

However, with a comprehensive end-to-end data capture system in the supply chain, not only would clinical studies work better and provide data for process development, it could also create efficiencies for the logistics process, ensuring supply integrity and, therefore, sustained consistency of the shipments, whether samples or drugs.

Looking at the technology evolution of the systems used for environmental condition detection in logistics operations, it might be thought that the environment has completely shifted to the late stages of evolution. However, while different stages are still in parallel use, there is a discernible movement towards the latter stages because of the additional benefits they offer, such as better process development capabilities and even corrective actions to prevent environmental excursions.

From Indicators to Internet of Things

Historically there were no means – or at least, very few means – to monitor environmental conditions such as temperatures during logistics operations. The simplest (and still widely used method) is to use indicators that show whether the temperature of goods has gone below a set limit or not. However, using this way of environmental monitoring lacked the ability to provide further analysis of what had happened and, more importantly, if the sample or drug had been compromised during the temperature excursion.

The next level of evolution produced continuous monitoring with a logger that travels with the monitored goods and stores all measured values in its memory. Originally, all loggers had to be handled manually after transportation, ie, their memory had to be read with a computer or other reading device. Nowadays, automatic solutions exist, using, for example, short-range radios to transmit data to a central system. While these automated solutions reduce the manual

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work significantly, they have one major drawback: the associated costs for the infrastructure needed.

When short-range communication is replaced with mobile data or even satellite connection, getting access to real-time information during transportation, not just once it has ended is possible. However, one big problem still exists, namely battery consumption. Mobile data (2G/3G/4G/long-term evolution [LTE] or similar) and satellite communications have not been designed for low-power devices and, therefore, larger devices with a lot of battery capacity have operation times ranging from days to a few weeks maximum. This may be sufficient on a transport-to-transport basis, but, from the point of view of a continuous logistics process, it causes a significant challenge when the device must be recharged or the batteries frequently replaced.

Fortunately, new communication technologies have been designed from an Internet of Things (IoT) point of view. This means that even the smallest IoT device is increasingly able to communicate with a cloud server. One of the ways this is approached is with narrowband (NB)-IoT and LTE Cat-M1 communication technologies.

This innovation utilises unused LTE frequency bands, called guard bands, to transmit small amounts of data. These bands exist inbetween LTE bands and can be easily adapted to communication purposes (1). While these guard bands do not provide enough bandwidth for a future where billions of IoT devices communicate with cloud by themselves, they offer inherent scalability as there are other frequencies available for NB-IoT and LTE Cat-M1.

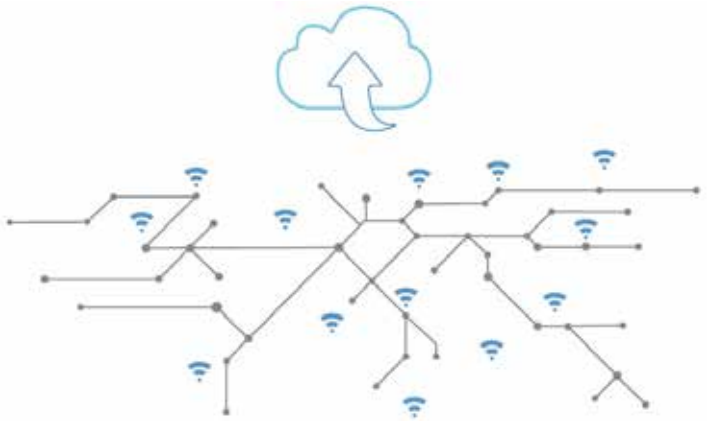
By using these communication technologies, monitoring of transportation temperatures online becomes trivial. There is no need for extra infrastructure when existing mobile network base stations are used to achieve real-time connection. The manual labour needed to collect information is virtually eliminated, and the communication protocol itself uses very little energy, meaning batteries can last for years.

What Better Time than Now?

Looking at these technologies, some differences are easily recognisable between them, the major being the ability to provide data in real time, as compared to those technologies which give out their data only after the fact. This then becomes a natural factor for choosing a technology for environmental monitoring in the study supply.

With highly temperature-stable drugs, it may be both easier and cheaper to choose a non-real-time logging option, because it is unlikely that anything could go badly wrong in the logistics process. However, with such pharmaceuticals and samples which would react adversely to temperature excursion, it might be wiser to invest in a real-time data collection system. This could easily help prevent any excursions from happening, thus saving costs and improving safety. Real-time technologies' capability of creating an unbroken record of electronic data and sharing this among multiple users is also a good way of managing the risks which often are found in logistics handover situations.

Real-time data capture could also enable easier home trial set-ups with safer direct-to-patient shipping. Considering



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that, in a 2017 study by CISCRP, 23% of participants felt the study centre was inconveniently located and 11% thought visits were too time-consuming, home trials could conceivably help with volunteer retention rates (2).

On a slight tangent to clinical trials logistics, a major pharma companies' working group already considers real-time data logging an effective way of preventing temperature excursions in last mile pharma logistics for controlled room temperature (3). Additionally, trials which are sponsored by these pharma companies could be expected to consider this a practicable approach for home trials.

Another point to consider is that, with real-time connection, it is demonstrably easier to achieve the kind of end-to-end visibility that can provide process development benefits, since the capability to collect data in a central databank already exists. Whether this should be done with one specific technology or a collection of many is dependent on the individual situation, but, arguably, the easiest way would be to adopt one technology for study-wide logistics, standardising the procedure of environmental monitoring to achieve comparable datasets. Multiple technologies can also be interconnected, as long as the gathered data can be proven to be equivalent.

Of course, it is not just demonstrating compliance with the regulatory environment, but, also, overall sustained quality management in operations which are the driving forces in pursuing as uniform sample and IMP conditions as possible. With real-time environmental monitoring, achieving both at once is easier.

Finally, the gathered data could be used to improve the clinical trial logistics landscape entirely if different stakeholders cooperated in a similar fashion as they already do in regard to clinical sites with the Investigator Databank (4). While sharing logistics data can seem counterproductive, considering that learning from mistakes means that someone has to make that mistake first, improved lane validation, packaging validation, and more could easily end up making the global logistics environment more sustainable across the board. Best-in-class solutions for various logistics challenges could be easily identified based on existing data.

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