IDMP integrity

Careful, robust planning and optimisation solutions must be employed to ensure a modern and future-proof supply chain, especially in the context of investigational medicinal products

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As trials become more global in nature, especially as they enter emerging markets, challenges intensify. To respond, pharmaceutical companies need to be thorough in their planning to be compliant and ultimately ensure patient safety. Today, we are seeing new and different regulations proliferating from global regulatory authorities. Long-concerned with GMP, regulators have been turning their attentions towards transportation processes and investigational medicinal products (IMPs) in the context of study conduct. This is a place where numerous GxP principles converge: GMP is a given, but it also includes the rules surrounding clinical excellence (GCP), good distribution (GDP), and storage practices (GSP). Cumulatively, these affect every aspect of the clinical supply chain.

Ultimately, these processes are critical because they ensure a product arrives in a useable condition in order to further the goals of the clinical trial and honour the safety of participants.

Maintaining integrity in transit

Many of today's IMPs require temperature control, especially in the realm of oncology and large molecule research. With clinical trial material, where knowledge of the stability profile is rapidly changing, there are risks involved throughout the transportation chain (usually outsourced and using generic, less well-controlled routes). It is critical to be aware of these risks, and a correctly managed clinical supply chain is paramount.

This is more complex than some manufacturers understand. Materials must be transported in controlled conditions (historically, this has been at 2-8°C, but there are expectations that ambient temperatures in the range 15-25°C are also actively

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controlled). These and other temperatures are possible using modern phase-change materials and making use of tools such as temperature-monitoring devices, temperature-controlled shipping containers and track-and-trace technology.

The aim is clear: whatever hurdles are faced en route, such as language barriers, variable climates, and complex import and export procedures, the IMPs must finish their journey in the same condition they began.

What is at risk?

If the supply chain is poorly managed, the trial's results are unlikely to be accepted. In the worst-case scenario, a company could be forced to discard millions of dollars worth of drugs, and patients will not receive much-needed therapies.

Temperature-sensitive IMP materials are handled and packed in a very specific way and must undergo appropriate testing to ensure the IMP is maintained at the required temperature – not just in transit, but also while it is in temporary storage. If it is held up in customs, the material must be treated properly to avoid any risks.

These risks represent a very real possibility. IMPs may suffer from temperature excursions, or worse, expire due to mishandling. If there is no way of telling when this occurs, it could place the end user in jeopardy. Therefore, companies need to put in place strategies to guarantee their products are not intentionally or unintentionally compromised.

Regulatory compliance across the lifecycle

Regulatory compliance lies in any company's best interest. Although most regulations don't pertain to one particular product type or storage class, the handling and release of the material is subject to stringent quality controls throughout the lifecycle of the IMP.

Examples of regulations to consider throughout the lifecycle include the European Clinical Trials Directive of 2004, which specifies that the IMP must fall under the control of a 'qualified person' (QP) who monitors the drug at all stages. The QP is educated in best practice procedures and possesses all the regulatory knowledge necessary to ensure full adherence of integrity of the IMP along the supply chain and through product lifecycle.

There are also regulations regarding good documentation practice, management, and import and export compliance. These ensure that the licences are determined correctly up front and that the product receives proper classification. They stipulate that trade agreements are employed, responsibilities clearly defined in writing, and qualification audits imposed – layers of risk mitigation that are unique to clinical trials.

This is completely differentiated from the language of commercial products. Since 99% of drugs used in such trials are conducted using an existing commercial product as a comparator therapy, it

is critical to handle the comparator therapy with the utmost care. Regional expertise in clinical trial conduct, import/export requirements, and regulatory compliance is paramount to successful transport of materials from the manufacturer to the patient.

When you are moving IMP from city A to city B, it becomes exponentially more complex when the transport is international. At present, there is no universally accepted set of standards, and though the last few years have seen some attempts at harmonisation, pharma companies are still compelled to deal with an extensive list of local requirements. For any company operating across borders, it is important to recognise how these rules differ from one country to the next.

Integrity of supply

In emerging countries, materials are very expensive to manufacture and purchase. They are also generally difficult to extract from the commercial environment, which compounds the issue. Manufacturers are reluctant to compromise existing patient supplies in support of competitive clinical trials.

When well-defined, postponement strategies (often referred to as 'just-in-time') can mitigate the risks of low inventory and multiple clinical trial demands. Specifically, postponement strategy entails that materials are labelled with minimal information, which enables the identification of the specific treatment and correct picking; however, regulatory compliant labelling is only performed against actual demand in a regional facility. This demand may be based on individual shipment requests or well-defined patient recruitment information, allowing the potential of sharing IMPs across protocols.

Country- and protocol-specific information are added as relatively less expensive single panel labels – mitigating the increased production costs against the procurement of multi-page booklet labels.

Labelling at this late stage also ensures appropriate expiration dates to be added, eliminating the need to extend dates in both central and investigator

inventory. The latter is particularly important considering the imminent changes arising with the implementation of the EU Clinical Trial Regulations and Annex VI.

It goes without saying that commitment from operational and quality team members is critical to ensure release and shipment can occur within 48 hours of the trial/country/patient-specific shipment request.

Takeaways

Maintaining good links to the supply chain throughout the clinical trial process is key to ensuring consistency across all sites and facilities. Companies should use electronic systems to their advantage, ensuring their operating procedures are the same in the US as they are in Singapore, for example.

Specifically, it's important to track the product from the onset to its final distribution at a clinical site. An operating model that provides complete visibility and the complete control of the supply chain will go a long way to ensure patient safety and successful administration of the IMP.

A modern supply chain solution needs to be carefully planned, tightly controlled, and seriously robust. Pharma companies should plan for all scenarios in order to minimise pitfalls and risks, reduce unnecessary expenses in the long run, and ultimately bring new medicines more quickly

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