Exploring the Complexities of Importer of Record to Develop Effective Global Distribution Strategies

The pharmaceutical sector's fundamental purpose of advancing human health and its ambition to deliver drugs to market as rapidly, safely and cost-effectively as possible has had a transformative impact on clinical trials management over the last decade.

This has given rise to globalisation. The average Phase III trial now spans 34 countries, with in excess of 1000 patients. Indeed, the number of countries serving as clinical study locations outside of the United States has more than doubled in the space of 10 years.[1] Not only has this been driven by cost reduction, with estimates suggesting that a clinical site in India can be up to 10 times cheaper than a US-based facility,[2] greater geographical reach equals more potential for study participants. This leads to faster and more effective patient enrolment,[3] which enables quicker, more cost-effective development and approval of investigational products.

Accompanying the rise in globalisation, and in part an achievement of it, is the development of biologics, which are predicted to replace 70% of small molecule drugs over the next two decades.[4] Unlike chemically synthesised drugs, biologics are incredibly expensive. Biologics also need to be processed and stored in controlled conditions, usually in refrigerated or frozen temperature ranges, and have limited stability data to withstand excursions.

When both trends combine, complexity manifests, risk increases and the margin for error shrinks drastically. A key element of the globalised clinical supply chain that poses a significant risk to a trial's timeline, patients and commercial viability is importer of record processes. Understanding the specific risks associated with the role of importer of record should be a core consideration at the onset of any clinical trial involving sites in multiple countries, especially those involving temperature-controlled products. Avoiding the pitfalls that lead to costly and chaotic customs experiences means developing effective distribution strategies that promote drug integrity and compliance.

Understanding the Role of Importer of Record

Obtaining a sound understanding of the role of importer of record is essential before effective clinical distribution plans can be designed.

Introduced as part of the Customs Modernization Act of 1993, the importer of record is responsible for ensuring imported goods comply with local law and regulations, and for payment of import duties, tariffs and fees.

The first point of contact should auditors require more information, regulatory responsibilities of the importer of record include evidencing that products have been manufactured and labelled according to country-specific requirements, are correctly branded and meet Good Manufacturing Practice (GMP) standards.

From an import perspective, the importer of record is also legally responsible – and financially liable – for accurate valuation, tariff classification, country of origin assurance, payment of import duties and taxes and effective record-keeping.

The rules on who can act as importer of record varies from country to country. Some countries dictate that only trial sponsors can fulfil the role, whereas others allow a third party to serve on a sponsor's behalf.

If sponsors choose or are required to operate as importer of record, a local office or associate can provide the 'boots on the ground'. If these options are unavailable or without an appropriate trading license, the sponsor will need to engage and grant power of attorney (or provide a letter of delegation) to a third party.

Examining the specific requirements of each country involved in a clinical trial will help sponsors to better determine their options.

Identifying the Common Pitfalls

Once the role, and how it relates to specific countries, is thoroughly understood, sponsors must familiarise themselves with some of the more common areas of risk. These typically relate to product classification, product valuation and the drug's country of origin.

When it comes to product/tariff classification, often referred to as a harmonised tariff code, it's important to remember that descriptions and values differ between product types and between active IMP and placebo. Placebos are often classified as a food component and are typically applicable to duty, which is usually between 6% and 12% of the product's value. Incorrect classification can lead to delays in customs clearance and mis-payment of duties. Contrastingly, active IMP is typically duty-free.

Of equal risk is the methodology used to determine a shipment's value. If customs are dissatisfied with the value declared on the shipment invoice, they will re-value consignments independently. This impacts the duty and taxes applicable to a shipment and can negatively impact trial budgets and timelines. It is no longer enough to apply a nominal value without appropriate methodology. Value evidence statement requests, to clarify how

product value has been determined, is becoming status quo for most customs authorities around the world – creating additional hoops for sponsors to jump through. The same is true when it comes to clearly and correctly declaring a shipment's country of origin.

Failure to provide the required substantiation in relation to tariff classifications, value methodologies and country of origin risks shipments being placed on hold by customs officials, while debates take place and the clock ticks on temperature-sensitive shipments. Equally, failure to appropriately manage processes and paperwork will cause delays that can compromise the integrity of temperature-sensitive consignments, introduce cost and negatively impact patients. Another point to note is that repeated non-compliances in these three core areas can result in more regular customs audits or financial penalties.

A World of Difference: Identifying Country-specific Nuances

Once the role is understood and core risk hot spots identified, it is necessary to drill down into the precise nuances in import/export criteria for each country involved in the global trial in question. Although there may be similarities, no two countries' import/export criteria are the same.

There is huge variation in import/export requirements. For example, the Ukraine sits at the more straightforward end of the spectrum. Newly introduced regulations remove the need for an import licence for both new and existing studies, along with a quick customs clearance timeframe of two to three days.

Countries in South America have more complex requirements. Some countries require an umbrella import licence that is valid for the duration of the study, but also require a shipment-specific import permit that needs to be obtained prior to shipping. This can take up to 50 days to receive, and customs clearance can take up to 30 days. Customs in Argentina require an import license that forms part of the annex to the clinical trial authorisation (CTA) submission. This can take 90 days to obtain. An import permit per shipment is also required and takes approximately four days to obtain. Customs clearance timeframes take 12 days on average.

China is also incredibly challenging to import clinical material into; involving highly regulated processes that require a local importer of record. Chinese customs authorities dictate that shipments are packed in advance, to obtain the weights and pieces information, which must be transferred onto the shipment invoice and physically verified by Chinese customs. Pack lists must also state the contents, number of boxes and both the nett and gross weight of the shipment. Meanwhile the type of import permit needed will depend on the product classification code recorded with Chinese customs. This can take between three and five days for a 'Q' permit and 30 days for an 'L' permit.

Adding further complexity, Chinese customs also demand a certificate of origin for all shipments, along with a chain of custody document that must contain the same batch number as the one shown on the shipment invoice. Shipments of IMP require transportation/movement documentation to evidence full transit from manufacturer to importer of record. A photograph of the drug label is also required, as is the sponsor's business licence and a guarantee letter to the BFDA confirming clinical trial approval.

If sponsors plan to import their IP to China, they should ensure products have at least 12 months' expiry remaining, or risk non-admittance. Equally, if trials involve temperature-controlled shipments, sponsors should expect consignments to be removed from temperature-controlled storage during customs inspection, which typically last between 24 and 48 hours. Managing the risk of excursions will need to be a key priority.

Understanding the variations of import requirements for each country included within a clinical trial will help form the foundation of an effective global distribution strategy, minimise delays, keep distribution 'on budget', and lessen the risk of negative impact to patient kits.

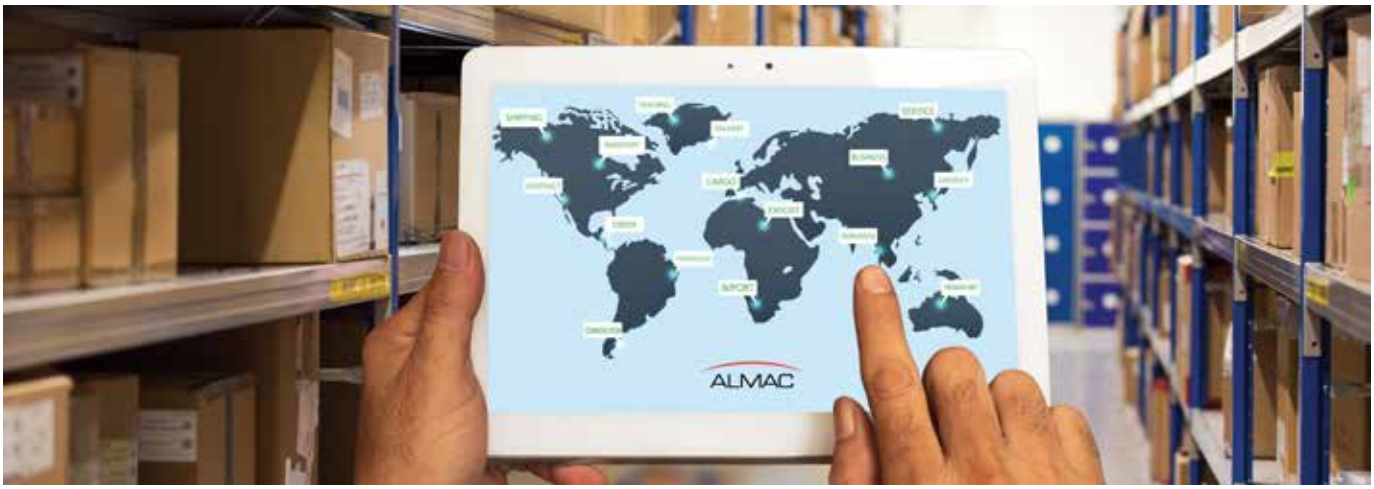
Embracing Importer of Record Best Practice

By exploring the variations in country-specific customs import/export requirements, it's clear just how complex developing a robust distribution strategy for a globalised clinical trial can be.

The ability to centralise all data pertaining to the lead times, documentation requirements and airport facilities of each country involved in the trial will help manage this complexity and reduce risk. Yet achieving holistic visibility of up-to-date import/export criteria, typical clearance times, customs facilities, duty and VAT liabilities and the recommended incoterms, which help establish where an importer of record's liability begins and ends, for 80+ countries, is a monumental task for sponsors to manage alone.

Furthermore, understanding the country-specific nuances of import/export criterial is only part of the battle. An importer of record will also need to build strong relationships with third parties in the global clinical supply chain.

Courier partners, for example, must have the skills and expertise to manage high-value, high-risk, time-critical shipments to countries



with complex import criteria. Partnering with an international logistics company with a global network and demonstrable knowledge and experience of import/export requirements within the pharmaceutical sector is a key responsibility for the importer of record. To form an effective link in the supply chain, selection criteria should assess a prospective courier partner's processes and standard operating procedures. It should also look at what controls exist within IT systems, the training of staff, drivers, and the security of vehicles.

Customs brokers also need to be selected by the importer of record, who will need to cultivate a global network of professional agents that can accurately prepare and submit documents for compliantly and cost-effectively clearing pharmaceutical shipments through customs. The customs broker must be licensed, have demonstrable relationships with custom authorities and be well versed in the nuances of pharmaceutical shipments; from laws and regulation to classifications, documentation and duties.

Despite multiple third-party involvement, the importer of record must maintain continuous oversight of drug shipments from the moment they depart a facility, until proof of delivery has been received from clinical sites.

A final branch of responsibility is meticulous record-keeping. During customs audits, officials will expect to review a complete record-keeping pack. An importer of record should have a sound understanding of what documentation must be contained within these packs. Customs will also expect importers of record to perform audits on their imports on a regular basis to identify errors in entry and allow for amendments to be submitted. For this to work, it is essential that trained, knowledgeable personnel are utilised to promote self-governance and compliance best practice.

Right Drug, Right Patient, Right Time, Right Temperature

A competent importer of record is a prerequisite to any successful global clinical supply chain. The role is vast and the remit wide, covering everything from liaison with third parties, troubleshooting delays, ensuring the correct tariffs and duties are paid, that all paperwork is present and correct and that drugs are released on time, to nurturing and co-ordinating global networks of couriers and brokers, contingency planning and compliance management.

While there is no one-size-fits-all approach, by understanding the key elements of the role, the risks, the country-specific nuances and what general best practice looks like, sponsors will be better equipped to develop effective global clinical distribution strategies.

Whether sponsors choose to manage the importer of record process themselves or outsource to specialists, by harnessing this knowledge and combining it with early, in-depth planning, the importer of record can play an essential role in delivering the right drug, to the right patient, at the right time and under the right temperature conditions.

In doing so, sponsors can embrace the benefits of global clinical trials and concentrate efforts on developing therapeutic breakthroughs that transform the lives of patients faster, and more effectively, than ever before.

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Sharon is an International Logistics Specialist having worked for 18 years in Clinical Supply Chain. She has expert knowledge in a number of key areas within the end to end supply chain process including management and control of temperature sensitive shipments; risk mitigation (identifying and managing risk); developing and managing robust relationships with transport partners; chain of custody responsibilities; active and passive shipping solutions and import/export country knowledge. Sharon has consistently delivered reliable and validated logistics solutions for customers based on her experience of establishing numerous international logistics models over the years. Sharon is passionate about providing excellent customer service in the area of logistics and this is demonstrated in her understanding of every role within the end to end supply chain process. She has first-hand knowledge of working with customers, external organizations and the appropriate departments within Almac to deliver well established logistics solutions in the Pharma industry. Sharon has travelled widely with her work and has been instrumental in the development of the logistics service provided by Almac.