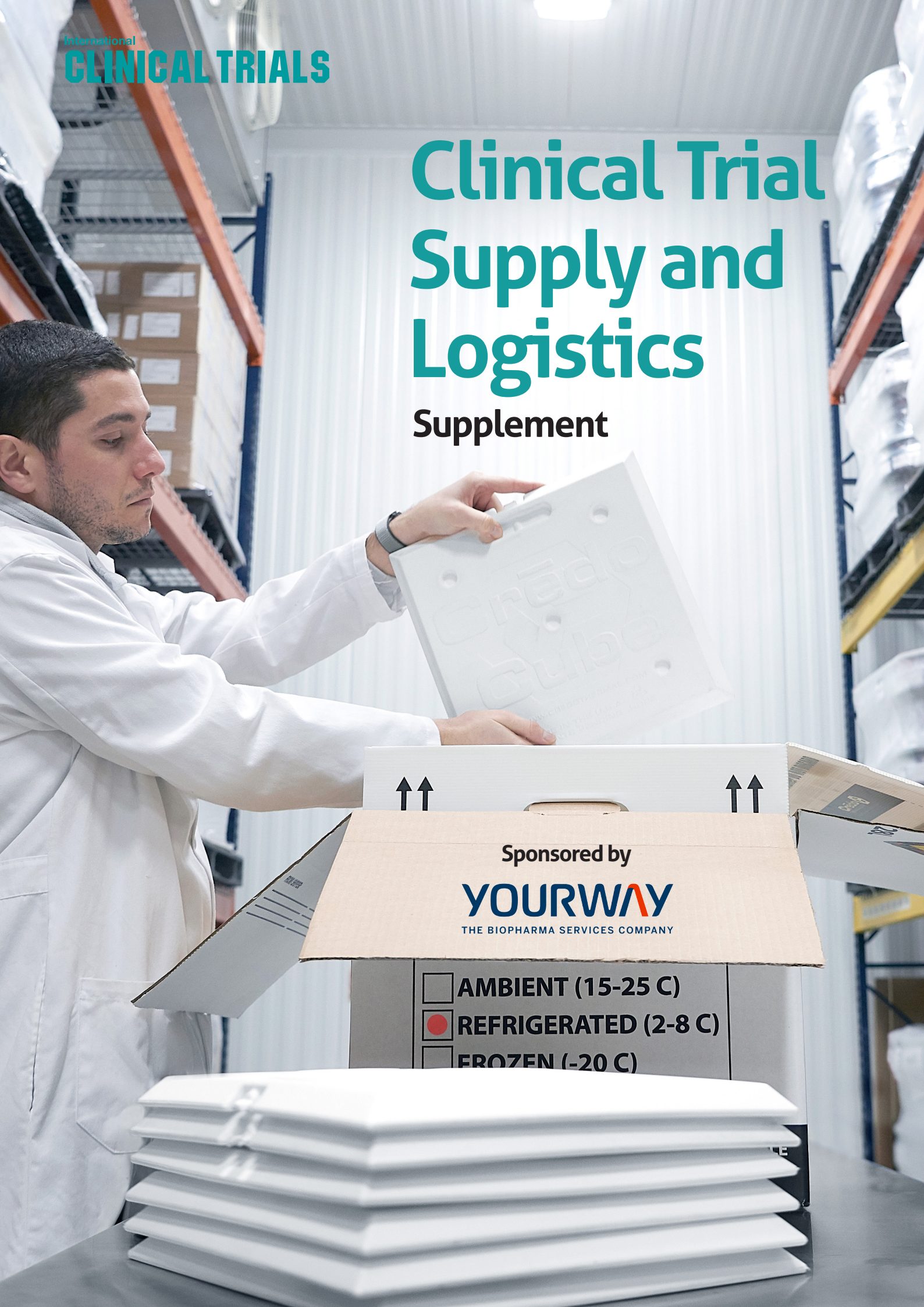
International
CLINICAL TRIALS

Clinical Trial Supply and Logistics

Supplement



Quality assurance and regulatory compliance, and ancillary supply chain management

The clinical trial ancillary supply chain (CTASC) is extremely diverse and complex. Although the CTASC has evolved dramatically during most recent years, one element holds true – CTASC performance has the potential to significantly disrupt trial timelines and patient outcomes

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The evolution of the clinical trial ancillary supply chain (CTASC), the globalisation and expansion of clinical trials in the most difficult regions of the world, and the requirement for better, faster and leaner methods, have presented a myriad of unforeseen and unprecedented risks and challenges for the CTASC organisation. The CTASC professional must possess the ability to research, evaluate, execute and guarantee that all components and all links in the chain align to achieve success.

Organisations that manage this supply chain must display proven, efficient and effective performance expertise in a variety of areas, including global distribution, regulatory compliance, quality control, product safety, risk mitigation and data integrity. Their teams must be subject matter experts in global sourcing, forecasting, inventory management, storage and product labelling, and have a firm understanding of import and export guidelines. Teams must have the distinct ability to develop customised approaches to fulfilment based on the region of the world where the chain will enter, and then modify these approaches when unforeseen events occur. Teams must have a distinct focus for the organisation's documented, proactive management of the CTASC, a focus that continues throughout the course of the clinical trial.

One of the most stringent deliverables that drives a successful chain is understanding all aspects of global regulatory compliance. The need for ongoing regulatory compliance surveillance is crucial when discussing and identifying the drivers of a successful chain. It is imperative that the CTASC professionals perform regulatory investigations, analyses and documented reviews for all medical devices, laboratory equipment, patient supplies and other regulations prior to placing a single item in a box for global shipment to a clinical site. Multiple regulatory compliance factors come into play that drive the overall outcome of the clinical trial ancillary supply chain. A sampling of factors are as follows:

1. CTASC organisations ship medical devices supplies and lab equipment to investigator sites participating in global clinical trials. It is necessary to provide standardised, registered medical devices supplies and equipment selected to fulfil the requirements of the protocol. CTASC organisations must embrace each country's medical device regulations and modify their processes to meet these directives
2. Product composition is critical for medical devices when discussing infusion lines and drug supply as an example. The medical experts in the CTASC organisation will develop product analyses, review regulatory concerns and then carefully select standardised items for use in all countries of the world
3. Formal documentation for calibration, certifications and in-country registrations/licensures must be available for regulators' compliance checks.

The CTASC brings uncertainties, complexities and pressures that are unique to the supply chain. Academic literature has proven, 'the greater uncertainty in the (supply) chain will affect the performance of the (supply) chain'.[1] The CTASC organisation must identify the regulatory compliance characteristics that contribute to increased uncertainties and complexities, and manage these throughout the supply chain. This vigilance and focus will influence supply chain outcomes.[2,3,4,5] So, considering all these demands in an ever-changing environment, how may the CTASC have these successful outcomes?

Measures for the successful management of CTASC

Effective management of the CTASC with all its complex and diverse deliverables is not a task for the faint of heart.

Although complying with global regulations is nothing new when importing and exporting goods across borders, vigilance is of utmost importance when managing a supply chain for a clinical trial. It is the responsibility of the CTASC organisation to understand and gather all documents associated with in-country regulatory compliance guidelines: product certifications; registrations; licensing documents; Ministries of Health approval documents; special requirements for UDI labelling of medical devices – the list goes on and on, item by item, country by country. Keeping abreast of the most recent regulatory landscape and changes as they occur across the globe are important considerations when managing the CTASC. Lack of ongoing surveillance, and assumptions based on previous successful releases, have the unfortunate potential to derail success of the supply chain.

Examples of regulatory agencies, directives and other verification guidelines or consultation purposes are per the summary below. It is important that the organisation managing the CTASC develops an organised reference checklist to confirm adherence to all country directives and guidelines prior to every global shipment released to clinical sites:

- Medical Device Regulation (MDR) in Europe
- In Vitro Medical Device Regulation (IVDR) in Europe
- Falsified Medicines Directive (FMD) in Europe
- National Medical Products Administration (NMPA) in China
- Korea Ministry of Food and Drug Safety (MFDS) in South Korea
- South African Health Products Regulatory Authority (SAHPRA) in South Africa
- Drug Supply Chain Security Act (DSCSA) in the US
- Global Atlas of medical devices (GAMD)
- European Regulation 2017/745, FDA Convenience Kit Policy.

Maintenance of an electronic in-house ‘Country Manual’ organised per region of the world serves as a reference point for quick analyses by the company’s regulatory compliance agents. Of course, this database must have active and ongoing surveillance checks to ensure up-to-date compliance information.

Overall, the CTASC organisation must embrace the importance of completing each step in the process of compliance verification, for a misstep can have profound consequences.

In addition to ongoing regulatory checks, it is imperative that CTASC experts understand the importance of country-specific product labelling for medical devices. The organisation’s quality control experts in the global supply chain must inspect and verify the product label prior to the release of goods to the field. For example, in Switzerland, the importation of a medical device with the standard European CE mark must include a CH-REP label.[6] This mark denotes the name and address of the individual who represents a manufacturing facility that resides outside of Switzerland who is responsible for formal issuance of product safety breaches, serious injuries, recalls, corrective actions and other announcements related to medical device concerns.

Although the CH-REP label is a requirement for all imported medical devices, CE mark is acceptable for goods exported from Switzerland.

Another example that illustrates the complexities in global regulatory compliance adherence involves those country-specific guidelines easily overlooked. Extreme diligence and review of regulations must prevail when attempting to import any goods into such countries as Argentina, Chile, Mexico and Brazil – the inexperienced CTASC team member may assume products or medical devices are approved for use in the country, when items will not clear customs.

Regulatory reviews must make note of the classification of products selected for distribution in the supply chain. For example, an energy or nutritional drink in one country will have clear passage across a country's border, while in others the drink, as a drug classification, requires a pharmacy licence. Proper regulatory reviews would have identified this concern prior to shipment and the CTASC experts would have had the opportunity to suggest an alternate with the clinical trial leadership. The CTASC is fraught with these, and hundreds of other potential mishaps, which impact the successful outcomes of the chain. These examples noted above clearly demonstrate the need for a hyper-focused diligence for regulatory compliance concerns within the supply chain organisation.

Conclusion

Robust regulatory checks are not a one-and-done exercise. Rather, global regulatory compliance processes must be a crucial component within the CTASC organisation. Standard operating procedures (SOP) governed by the quality assurance and regulatory compliance units in the organisation must document appropriate processes and checklists to guide team members. These processes must illustrate redundant and replicable procedures applied during each phase of the clinical trial. SOP must include documented training, assessments and evaluations of all CTASC team members with a robust set of key performance indicators to ensure compliance. Surveillance of the organisation's Country Manuals, and updates as regulations change, serve as the roadmap for CTASC team members to achieve success. Only with extreme focus and dedicated alignment is success achieved. For, it is not just above shipping 'stuff' across the globe – the 'stuff' included in the global shipments in the CTASC has the potential to touch the sickest of patients looking for cures to what ails them, and the supply chain is responsible for its outcome. The key is to ensure the CTASC does not negatively impact the clinical trial outcome or soundness of its results.

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6. *Visit: swissmedic.ch/swissmedic/en/home/medical-devices/market-access/ch-rep.html*

Dr **Joanne Santomauro**, chief executive officer and founder of **Ancillare**, created the CTASC management industry in 2006. Joanne successfully completed the Committee of 200 Growing Entrepreneurs Program in 2005, the Tuck School of Business Executive Program in 2008 and she is the recipient of the 2011 Enterprising Women of the Year and Marcum's Innovator of the Year awards. Joanne also serves on the YMWIC Foundation Board, a STEM programme dedicated to the advancement of science, technology engineering and maths for middle through high school students. She also serves on the DCAT Alliance for Industry Women Committee to develop special events and programmes to educate, inspire and empower women in the pharmaceutical industry.

Barbara A Falco, vice president of Quality Assurance and Regulatory Compliance at **Ancillare**, is an accomplished senior executive, board member and consultant with more than 35 years of success. Throughout her executive career, she has been responsible for business development, creating quality management systems and managing supplier company relationships. Barbara also has extensive experience managing and auditing suppliers, as well as a background working in quality assurance and control in the API industry. She spent over ten years on the board of directors of the International Pharmaceutical Aerosol Consortium (IPAC-RS), where she served as the chair of the supplier quality working group that developed and published (2006 & 2011) guidelines for orally inhaled and nasal drug product component supplier quality.

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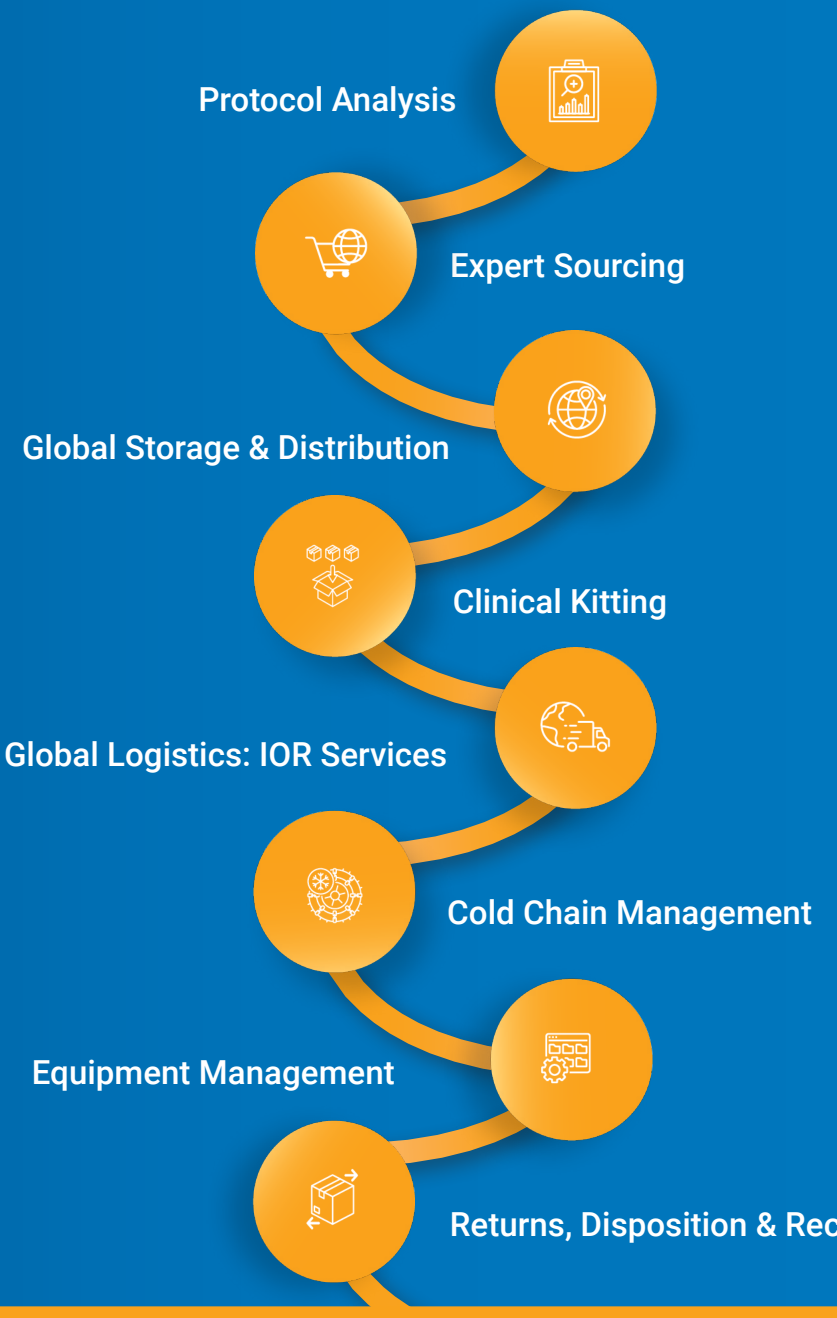

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