Standardization & Risk Management In Cold Chain



ColdChainIQ
Temperature Control Logistics & Quality Network

14TH COLD CHAIN GDP & TEMPERATURE MANAGEMENT LOGISTICS GLOBAL FORUM

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Ahead of the 14th Cold Chain - GDP & Temperature Management Logistics Global Forum, Cold Chain IQ looks at the concept of global standardization with risk management in the cold chain. This whitepaper explores supply chain security and validation as they pertain to lane qualification, data monitoring, shipping lanes and stability budgets.



Supply Chain Security

There are a number of challenges faced when it comes to achieving worldwide standardization of supply chain security within the cold chain. For example, complications are encountered with the level of international regulatory convergence that is required. Brian Johnson, Senior Director Pfizer Supply Chain Security explained: "It's manageable to get industry standards in place and get scientists to agree in best practices. [However], getting those best practices transformed into regulations and legislations around the world and getting standardization between governments and regulators is difficult [as well as] finding standards that are applicable to very different economies around the world."

With local infrastructures placing such a blockade on creating a global standard, Charles Forsaith, Director, Supply Chain Security, Purdue Pharma LP notes that TAPA's set of facility security standards with chapters dedicated to different regions represent quite possibly the closest reality to a global standard the industry will see. As TAPA is a voluntary membership organization, the body is unable to impose those standards on companies beyond a certain extent. Common terminology is another roadblock for synchronizing international efforts. Standards and certifications are needed to provide common definitions and improve understanding.

Which leaves the question: What would the by-products be if the industry dropped the mission to deploy standards for international supply chain security? Experts note that this would result in seeing counterfeit medicines enter the supply chain – placing critical risk on patient safety. Firms would also run the risk of having shipments stolen and being left unaware of when or if the shipment is recovered – another significant risk. These prospects highlight the importance of fully knowing your partners of choice for the cold chain maintenance and security of your shipment.

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In maintaining the mission to improve global security standards, membership to trade associations and local initiatives will be key. Charles Forsaith notes that this will allow members to participate in helping achieve standards and validating supply chain security in various regions.. Brian Johnson encourages all stakeholders to engage in working with regulators, governments and law enforcement bodies to assist with the development of legislation and regulations around the world. He adds that, in the creation of legislation and guidance, regulators should strive to implement a holistic approach, simultaneously considering cool chain, supply chain security and falsified medicines and GDP matters.

This wider view will be instrumental in combatting emerging threats. Packaging professionals are often trained in process and quality improvement programs to narrow focus to a set of key factors that reduce vulnerability. While such focus may be efficient for root cause analysis and refinement of operations, it may be the wrong method to address emerging or evolving threats.



The narrowing of focus results in the testing of fewer places, opening more opportunities for counterfeiters to act and not be detected. Having too narrow of a product counterfeiting focus can be inefficient at best and catastrophic at worst.

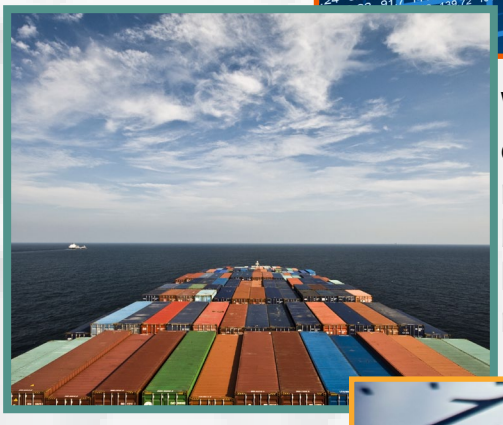
Anti-counterfeiting standards and certifications will continue to evolve and provide effective best practices. Efficiently meeting emerging laws and regulations will continue to be important, but they should not be a distraction to existing business risks. Understanding impending regulations and standards are important but there must be a focus on mitigating specific business threats that may already exist. (1)

Validation & Lane Qualification

Industry figures have called for increased market consensus on the risk assessments a lane qualification should contain.[2] Dr Rafik Bishara, Ph.D, Technical Advisor, Retired Director, Quality Knowledge Management and Technical Support, Eli Lilly and Company has stressed the need for an industry task team for lane qualification – with the benefit being that standards can be outlined to specify required handling, storage and distribution to the patient.



However, some industry commentators have highlighted that standards would need to be flexible to allow approaches to be tailored to specific scenarios. These stand-alone cases would require the end user to invest in analysis to assess the most effective method for transit and temperature profile. In a recent article Kevin Kohleriter explained: "The problem is that one size fits all does not work. You are not trying on a hat or a pair of gloves; you are shipping a sensitive, costly product affected by the type of packaging you use, the amount and type of refrigerant, the transport mode, the length of storage and transit, not to mention the sensitivities of the product itself. Think about it. If you are shipping your product from New York to Texas in the winter, there are very different criteria required than shipping an overnight package from New York to Chicago. So why would use the same criteria for both?"



When increasing the understanding of a certain route and the ability to navigate its risks, the application of both continuous monitoring and lane validation is a key tactic for robust lane qualification.



Risk assessments also need to establish transparency on the network of professionals who support the product through the cold chain. Jim Bacon, Cold Chain IQ columnist, illustrated an exercise which embodied this that was implemented in his time at Grifols. The Mock Shipment Call was a method used



to eliminate risk and qualify the lane by having every single stakeholder on that lane present to clarify and run-through their role in the chain. He commented:

"All too often, an excursion can be attributed to some form of human error and more often than not this occurs during a transfer or hand-off from one service provider to another. I have addressed this issue in many presentations over the past many years, referring to it as "the weakest link.". Shippers that improve these hand-offs through robust and disciplined process steps and improved agreements with providers have mitigated their risk by securing "stock throughput coverage" insurance which provides continuity coverage for shipments. This however does not eliminate the risk, so extra steps and a continuous loop of review is required.

"More recently, due to increased regulatory scrutiny, shippers have engaged in lane qualification, serving to document the process, test and approve with live data. Through collaboration with our cold chain partners, we have taken it a step further and engaged in a process we call "The Mock Shipment Call". This is a tele-conference call we engage in before agreeing to execute a live shipment for a new shipping lane." (3)

Data Monitoring in Shipping Lanes

Global regulatory authorities place emphasis on evidencing control over distribution environments. Here, an alignment between shipping conditions and thermal protection packages and their respective parameters, including shipping time and min-max profile temperatures. Data that is enriched with as much information as possible is seen as the key to ensuring regulatory compliance with many using data logging technology to meet tightened shipping requirements. For example, RFID technology offers passive tags that can be read at certain points, or active tags that submit a periodical signal. (4)

In creating a statistically accurate transport model Cold Chain IQ columnist, Kevin Kohleriter explains that this can be obtained by collecting data from every required shipment, season, and location. This has led some to apply data loggers to



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thousands of shipments, however in some cases this can be shortened from a period of months to days. Data loggers can be used on the inside and outside of the pack to correlate the actual ambient temperature to the profile used to double check if the actual profile of the system matches the data model and standards. This assists in building performance qualification criteria for seasonal temperature and lane mapping studies. These studies can allow firms to make evidenced improvements to their shipping lanes.

The practice of data sharing is labeled as important for smoothening clinical logistics. Various units of data are available to be shared – stability data, required duration and volume. Dr.Bishara maintains that the sharing of this data will allow for optimized storage and distribution guidance as well as the containment of risk in some places. This sharing will also help provide harmony by contributing to making industry standards.
In regards to the sharing of knowledge to aid the industry's best practice definitions, Carlos Castro, Cold Chain / Transportation Project Manager for Bayer Healthcare, notes: "In terms of harmonization for the global supply chain of pharma and biotech products, I believe the challenge is in mature markets – US, Japan, Europe. The infrastructure is there. The awareness from the supply chain links is great, but as pharma and biotech components move overseas to emerging markets or are growing rapidly at rates between 20-30%, the challenge [is] that we still don't have infrastructure to support cold chain and the knowledge is still not there.

"I believe the next frontier we need to cross is summarizing [the supply chain knowledge] in these emerging markets as well as improving and establishing a baseline for cold chain facilities." (5)

Stability Budgets

The need for heightened awareness and use of stability budgets within cold chain has been stressed in the industry of late. In a recent article Dr. Bishara and Dr. Erik J. van Asselt explained that a stability budget:

"Refers to the quality of a product to resist, under specified conditions, irreversible change in its identity, strength, quality, and purity at various temperatures above and below the labeled claim storage temperature.

".... [The drug degradation] rate depends on several factors including but not limited to the physical and chemical properties of the active pharmaceutical ingredient, formulation, pH, temperature, water and oxygen sensitivity, light sensitivity and primary packaging." (6)

In explaining the importance of deploying a stability budget, Dr. Bishara noted that "the effect of not knowing your stability budget, calculating it correctly, and most importantly, implementing it on a quality-based standard, is that you may discard medicines and vaccines that are good – or approve the utilization of pharmaceuticals and vaccines that have been exposed to excursion that has resulted in the degradation, lack [of] efficacy and potency. So by knowing your budget, calculating it correctly, and implementing it during the supply chain in case there is a deviation or an excursion heat or freezing you will be able to make quality-based data decision on what to do with this material." The time out of storage (TOS) can then be calculated and compared to allowable excursion time.

Packaging and manufacturing stages can be conducted in ambient temperatures for cold chain products by using the allocated TOS, then manufacturers can benefit from improvements felt in machinery performance and employee performance. However, this may impact the product's shelf life, so this time used needs to be measured and balanced. Hazards within transportation represent larger threats to the cold chain with the prospects of physical contact, handovers



and unforeseen delays, so the TOS can be useful in managing temperature excursions.

The PDA's guidance, especially the technical report number 53,on stability budget and correct application of the method has been praised for its contribution towards global standardization. Dr. Bishara noted that to shirk the use of a stability budget could be perceived as an indicator that professional is not following modern industry best practices. Regulators are likely to enquire about stability and the protocol deployed to generate the data and the implementation of a stability budget. Rafik stresses that to avoid implementing a stability budget is in fact taking on a risk – dependent on the inspector they are allocated and whether that inspector decides to focus on the stability budget.

Dr. Bishara also stressed that this year's 14th Annual Cold Chain GDP & Temperature Management Logistics Global Forum stands as an excellent platform for industry members to gather and discuss ways to advance industry standards.

Rafik Bishara, Brian Johnson and Charles Forsaith will all be presenting at this year's Cold Chain Global Forum, taking place September 26-30 in Boston.

Acknowledgements

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Rafik Bishara, Ph.D, Technical Advisor, Retired Director, Quality Knowledge Management and Technical Support, Eli Lilly and Company

Brian Johnson, Senior Director, Supply Chain Security, Pfizer Global Supply

Charles Forsaith, Director, Supply Chain Security, Purdue Pharma LP



14TH COLD CHAIN GDP & TEMPERATURE MANAGEMENT LOGISTICS GLOBAL FORUM

September 26-30
Hynes Convention Center | Boston, MA

The world's largest event for temperature-controlled life science supply chains will return this year with extended topic focuses, session formats, speaking faculty and vendor options. Update and adapt your supply chain processes to tackle future challenges and ensure maximum compliance and quality at minimum cost.

With constant evolving regulatory requirements across the globe, the 14th Cold Chain GDP & Temperature Management Logistics Global Forum will help your company balance quality, risk and cost to achieve compliance and maintain product integrity.

Join us to:

- **Deepen your cold chain knowledge through hands-on exercises** in our in-depth pre-conference master classes and workshops
- **Ask one-on-one questions of our expert speakers** during dedicated post-session Q&A in our Exhibit Theater
- **Work towards greater industry standardization** in stability data sharing, supply chain security and packaging qualification in our reinvented Blue Sky Room
- **Forecast future regulatory trends** from our senior panel of international regulators from the United Kingdom, United Arab Emirates, Austria and Zimbabwe
- **Build new business relationships with other international attendees from 27 different countries** during our targeted networking sessions, cocktail reception and numerous group activities
- **Make informed purchasing decisions** by comparing the latest cutting-edge temperature-control solutions in our expanded exhibit hall.

Download Agenda

www.coldchainglobalforum.com

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Resources

1. http://www.coldchainiq.com/supply-chain-security/articles/anti-counterfeit-countermeasures-tactics-evolving
2.http://www.coldchainiq.com/quality-management/white-papers/lane-qualification-vs-continuous-monitoring-2015-r
3. http://www.coldchainiq.com/transportation-logistics/columns/the-human-side-of-lane-qualification-the-mock-ship
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