GLOBAL MASTERY

eBook

Balancing Quality, Risk and Cost to Achieve Compliance and Maintain Product Integrity

PHARMA LOGISTICS WEEK

CONTENTS

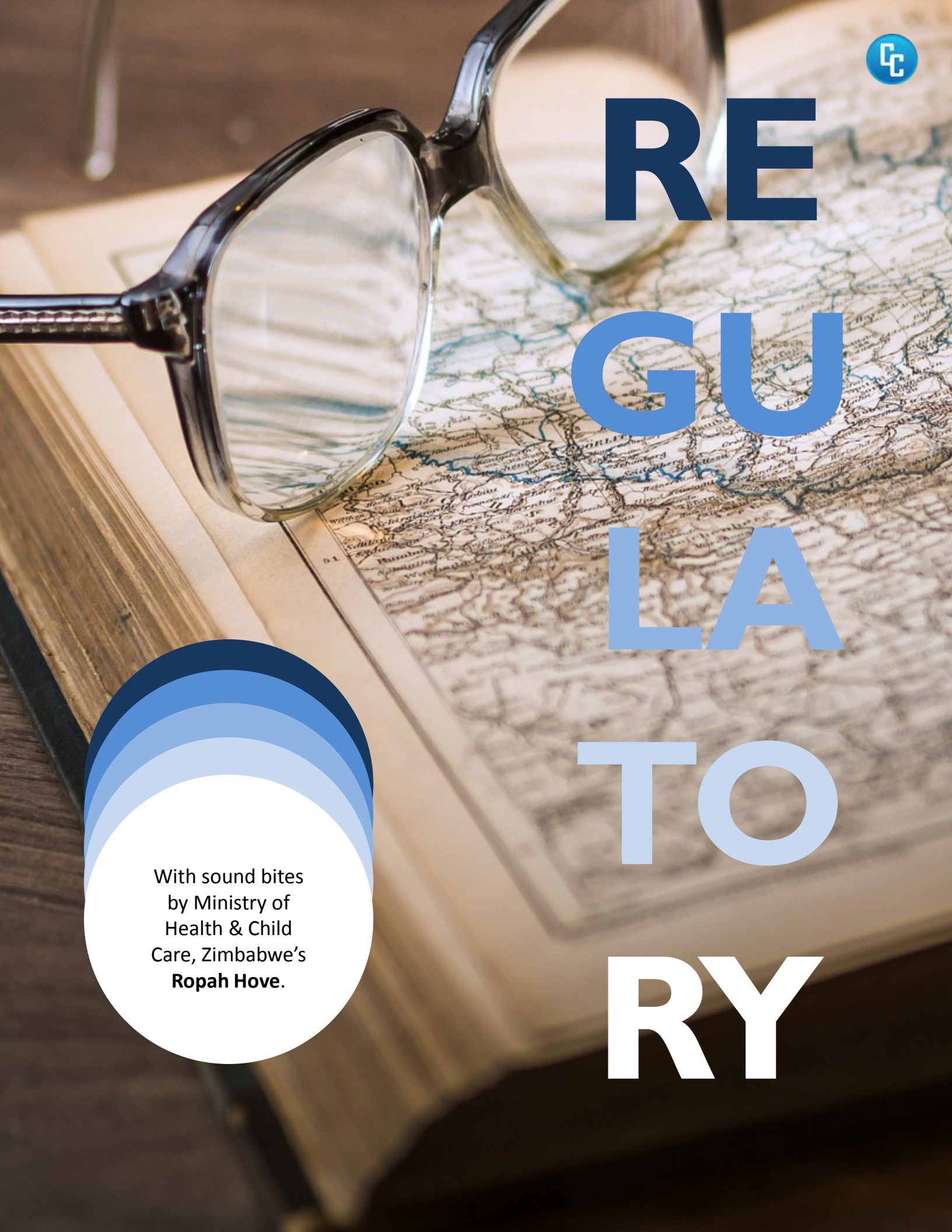
THE COLD CHAIN

is in a state of flux as a result of the meteoric growth of the healthcare industry and the equally rapid emergence of new and unclaimed markets. If you're not innovating, then you're already behind.

Cold Chain Global Forum

SPRING . 19

Temperature Controlled Life Science Supply Chains



REGULATORY

With sound bites by Ministry of Health & Child Care, Zimbabwe's **Ropah Hove**.

"Vaccine shipments in Zimbabwe face significant challenges. I'll explain how our health Ministry has taken several important steps recently to improve last-mile vigilance in remote and developing regions, with the ultimate goal of maintaining patient integrity right up to the point of administration."

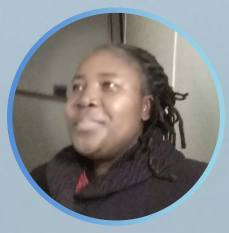
Ropah Hove

Director, Pharmacy Services ● **Ministry of Health & Child Care, Zimbabwe**

SUMMIT SESSION

Maintaining Vaccine Integrity at Various Temperatures in Remote Areas

- Utilizing gas and solar powered refrigerators to store cold chain products in hard-to-reach regions with limited electricity
- Assess the impact of data loggers, implemented in Zimbabwe in 2015
- Evaluate the quality of product stability data, and the conditions under which those data were generated



What are some of the main difficulties you see in maintaining vaccine integrity in Zimbabwe, especially in remote areas?

Hard to reach regions of the country have limited access to electricity for the refrigerators and untarred roads. During the rainy season when it becomes necessary to transport the vaccines to an alternative site, the unpaved roads are inaccessible hence presenting further difficulties for maintaining product integrity.

What are some of the key solutions to these issues?

The utilization of gas and solar powered refrigerators to store vaccines in hard to reach regions with limited electricity.

There is currently a lack of clarity from regulatory bodies, which makes achieving global standards difficult. How can this issue be alleviated?

More engagement and dialogue to explore practical solutions for resource limited settings.

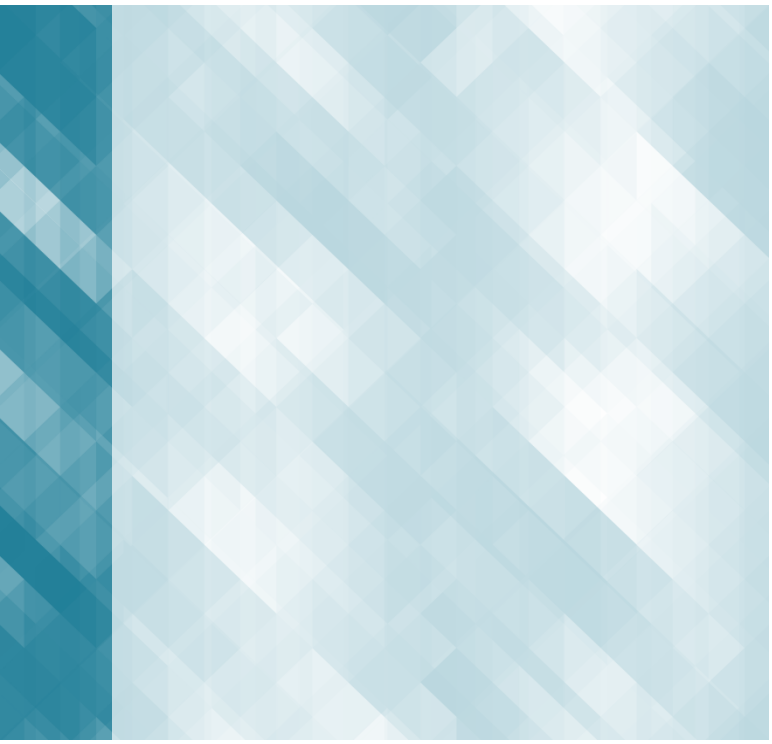
Pictured: Harare, Zimbabwe

PACKAGING

Discussed by:
Dr. Bernard McGarvey

ELIMINATE
KEY FAILURES

with **Dr. Bernard McGarvey**,
Senior Engineering Advisor
Eli Lilly and Company



Doctor Bernard McGarvey is a Sr. Engineering Advisor responsible for process modeling applications at Eli Lilly and Company. He supports the application of process modeling in both manufacturing and process development. He has thirty two years' experience in manufacturing where he has held positions in process engineering, process control engineering, and technical services.

During your session, you will discuss the current approaches to selection of passive shippers and how they can fail. What are some of the key reasons for failure?

The key failures I want to focus on are:

- We develop OQ ambient temperature test profiles that are not representative of the actual conditions that the container will see during distribution/logistics channels and so failures could/will occur.
- We use such conservative OQ profiles that we overdesign – not a failure of the container as such but more a failure of the design process.

What are container performance curves, and how do they fit into the package design process? What are some of the concrete benefits you've seen from using them for passive shipper development/qualification?

A container performance curve is a simple way to summarize the expected performance of a container over a wide range of ambient conditions. It is an analog to equipment performance curves we use every day to design engineering equipment like pumps and valves. One of the values we have seen is that it can quickly communicate whether the container is suited to the specific shipping lanes it will be used. This also helps show that we are tuning our design to the thermal demands being placed on the shipper.

Performance curves can identify performance capabilities and theoretical temperature tolerances (guard banding limits) for each design.

Cost is always a concern in this very expensive field. How do you engage in robust design strategies without overdesigning at extra cost?

To me this is the key. It's easy to come up with a cheap container that does not work or an

expensive container that is over-designed. Navigating the space in the middle is where the focus needs to be. For me is all about approaching a shipping container like we do all other equipment – it is basically an engineered system that works on the basis of the first principles of heat transfer and thermodynamics – principles that are well understood.

I do not believe we can get to better cost/performance balance without designing containers on the above basis. And what we always have to remember is that the container must protect on both the hot and cold side so bigger is not always better. Adding more frozen packs may improve your hot side performance but what does it do on the cold side?

I also think that you should start out letting the vendor optimally design a solution without any limitations. This provides you with an operational and cost effective baseline. Any limitation placed onto the system during the design process can then be quantifiable and rationalized during the design process for optimization. Tradeoffs can be understood and negotiated between operations and business (financial).

What are some of the key factors you consider when auditing pre-qualified boxes from suppliers?

My main interest is in seeing if the ambient temperature test profiles used in the vendor's OQ are sufficient for our needs. Irrespective of how the vendor arrived at these profiles, we use our internal criteria to judge these profiles. If they pass out criteria then we can move forward.

Note that we may also decide based on what the vendor used that the containers are overdesigned and this may represent an opportunity for optimization.

How does your qualification method support the reuse of passive containers that were originally designed for single use?

Only insofar as any re-use protocol must show that the containers can protect against the same thermal challenge as we identified for the original OQ after the intended number of re-uses. I do think it's a good idea to be thinking about re-use potential from the beginning – when the container is originally being chosen.

The performance curves could also quantifiably compare performance capabilities amongst different components, maybe some more reusable than others. Then a determination based on operational and business benefits can be assessed.

Using Performance Curves to Define OQ Test Profiles and Optimal Designs for Passive Shipping Containers

Dr. Bernard McGarvey
Sr. Engineering Advisor
Eli Lilly & Company

CO-SPEAKER:

Paul Harber
Principal
Modality Solutions


LOGISTICS
Perspectives from:
Dana Dallas
and
Lisa Baker

STABILIZE YOUR DATA TO PREVENT SUPPLY CHAIN FAILURE

DANA DALLAS

is Cold Chain Program Manager at the Defense Logistics Agency Troop Support Medical. She began serving her country as a United States Air Force Academy graduate, using her Biology/Pre-Medicine degree as a Healthcare Administrator and Medical Logistician with the United States Air Force, still serving her country as a Major with the 914th Aeromedical Evacuation Squadron today.

Dana, what are the most common external factors that cause pre-qualified packaging solutions to fail, in your experience?

Most pre-qualified solutions are designed according to standard temperature profiles, but in many cases, the actual thermal profiles for the transit lanes you are moving in vary greatly from the "average" profiles. For example, if you are using a profile where the max ambient exposure is 82ºF, but the carrier's Distribution Center warehouse averages a temperature of 107ºF during the summer months, no matter what your pre-qualified packaging solution is validated to, it won't make it the full duration...2-8ºC for 72hrs can very quickly turn into 2-8ºC for 24 hours…

In that same vein, another challenge I see with commercial-off-the-shelf solutions (COTS) are Universal Pack-Out designs. For domestic shipping in pretty mild ambients, they work great, and they are very simple to use from an operations standpoint...but for international shipping, or shipping during extreme temperatures in the summer and winter months, the upper and lower limits of the validation are stretched to their limits, and sometimes past.

That being said, even with seasonal pack-outs, you still have the challenge in trying to "predict" the ambient temperatures at the end destination...all your research tells you that it is going to be 70ºF when the package arrives in 3 days, and then a nor'easter swings in unexpectedly and your ambients bottom out at 50ºF. You've now got too much frozen coolant in the box, but in many cases it's too late to do much about it.

How can this be combated?

Our program has been experiencing difficulties in moving cold chain material, using our pre-qualified packaging solutions, from our distributors on the West Coast to our military treatment facilities overseas in the Pacific Rim. What we ended up doing was hiring an engineer to thermally map each of our transit lanes from California to Japan, South Korea, Guam, and Okinawa. We then took the most challenged supply lane of those 4 and had the engineer apply them to our pre-qualified solution to find the specific failure points. They then modified the packaging solution to make it specific to our transit lane (vs. sticking with the original standard temperature profile they were designed against).

Additionally, I am a huge proponent of the use of temperature monitoring devices (of some kind) in all shipments...regardless of how the transit time may be, regardless of the modality, and even when you have a pre-qualified solution. Pre-qualified solutions are deigned against a certain set of parameters that all have to be in place for it to perform the way it is supposed to...but it is a dangerous assumption to assume those are never breached, and when they are, having a temperature monitor in the shipment will 1) allow you identify it clearly and 2) allow you to use stability data.

What's the most important consideration for successfully quantifying the risk of failure within specified lanes?

Knowing exactly what the thermal profile looks like that your pre-qualified solution was designed against, and know whether that will closely mimic your supply lane or not. And you have to have firm, clearly laid-out Standards of Operation with each partner in that supply lane that is going to touch your shipment...and ensure they are trained and understand it completely.

Do you find your peers use their stability data effectively when putting together a strategy to stop excursions?

I find from the manufacturer level, they tend to use as much of their stability data as they can in their initial transit lanes...whether they are shipping to medical treatment facilities or to distributors. Often times, this results in the initial shipping leg being done "off-label" (i.e. shipping an item that is FDA labeled as frozen in a refrigerated pack-out for the initial supply lane, or vice-versa). The down side to that choice is that it often leaves the distributor with no excursion allowance remaining for their portion of the supply lane.

Now that being said, there are many manufacturers in the industry who have done an excellent job in quantifying how much stability data is allowed during manufacturing, how much is allowed in distribution (even through multiple moves), and in many cases how much is allowed at the facility/patient level. Rather than focusing on stopping excursions (which truly may not be a realistic proposition), they apply a certain amount of focus on minimizing excursions and having the data available to still release the material for use.

How can stability data be used to its utmost?

You cannot assume that zero excursions, a perfect 2-8ºC shipment (for example) each time, is going to be the standard...it can certainly be your goal and what you design the program to try and meet...but having extended stability data in place that can be utilized when/if something does go wrong, unplanned, etc. is extremely helpful. It prevents sites from having to discard material unnecessarily, or on the flip side, ensures they do not use material that has reduced efficacy.

What are the regulatory restrictions associated with its use?

Technically speaking, no manufacturer is permitted to recommend the use of a product that has been exposed to an environment other than what is indicated in the Package Insert as part of their licensure...and many manufacturers choose to adhere to that specific letter of the "law" when it comes to sharing what stability data they may have, if the even chose to make the investment to conduct the studies to establish extended stability data. Many laboratory supply manufacturers, for example, do no studies whatsoever outside of 2-8ºC...or if they do, they only stress the product to 15ºC and/or for 24hrs, and then stop. Now that being said, there are many manufactures in the industry who have made the decision that although they cannot recommend use outside of 2-8ºC, for example, they will share what data they do have and the entity asking the question can take that information and make their own decision, with no liability applied to the manufacturer. While some vendors have found somewhat of a "happy medium" in that they will not share the specific stability data, they will take the specifics of the case involved, and let you know whether their data does or does not support use...and then once again, you can make your own decision based off of that (preceded by the standard disclaimer, of course).

There are many emerging markets for pharmaceuticals which may have poor infrastructure. How do you mitigate these challenges when shipping over 300 distinct cold chain products to remote regions all over the world?

The most productive thing we can do in mitigating those challenges is constant communication between all players within the supply lane. The distributor initially packaging the shipment and hiring the carrier for movement has to pre-alert the end customer that it's coming, how it's coming, how it's packaged, what they need to do as part of their receipt, etc. The end customer then needs to take that information and coordinate with their local carrier rep, start pre-clearing the shipment through customs, etc. When we ship "blindly" is when we have the most issues.

Additionally, as much as I would like to say that we can literally ship everywhere in the world, there are some locations that we just do not and/or cannot ship to. It is important that you vet all possible delivery locations: Can the carrier get there? How fast can they get there? What are the capabilities for

refrigeration/repackaging if there is a delay? Does the receiving site have refrigeration capability upon receipt? Does that specific country have unique/special considerations for clearing customs?

What is your expectation for the next five years?

I think we are going to see a VERY strong increase in the focus on Controlled Room Temperature shipping, especially at the Distributor level. I expect manufacturers to really start drilling down on their distributors and their storage capabilities for CRT: Are their warehouses qualified for CRT storage (vs. just Room Temperature)? Are they cross docking my CRT products at 15-30ºC/20-25ºC, or are they just shipping at whatever room temperature ambient it happens to be that day? I think the fact that the FDA does identify a difference between CRT and Room Temp is going to become somewhat unavoidable. The industry was focused on refrigerated and frozen shipping for so long, but that is almost "old hat" now...we really need to start focusing on the elephant in the room, the CRT items that are truly being treated as Room Temp.

Methodologies for Assessing Failure Modes and Root Cause Analysis of Temperature Excursions

- Match transit/carrier details with time/ temperature data from temperature monitoring devices
- Understand all possible external factors that could cause your qualified packaging solutions to fail Dana L. Dallas, Cold

Dana L. Dallas, Cold Chain Program Manager, Defense Logistics Agency Troop Support Medical

Amgen recently switched to a temperature monitoring plan across multiple lanes and seasons.

We asked Lisa Baker, Director, Supply Chain – Amgen, about...

TAKEAWAY

Performance Verification using Temperature Monitoring Plans meets regulatory expectations by showing evidence of shipper and lane performance in actual conditions.

BIGGEST CHALLENGES

1

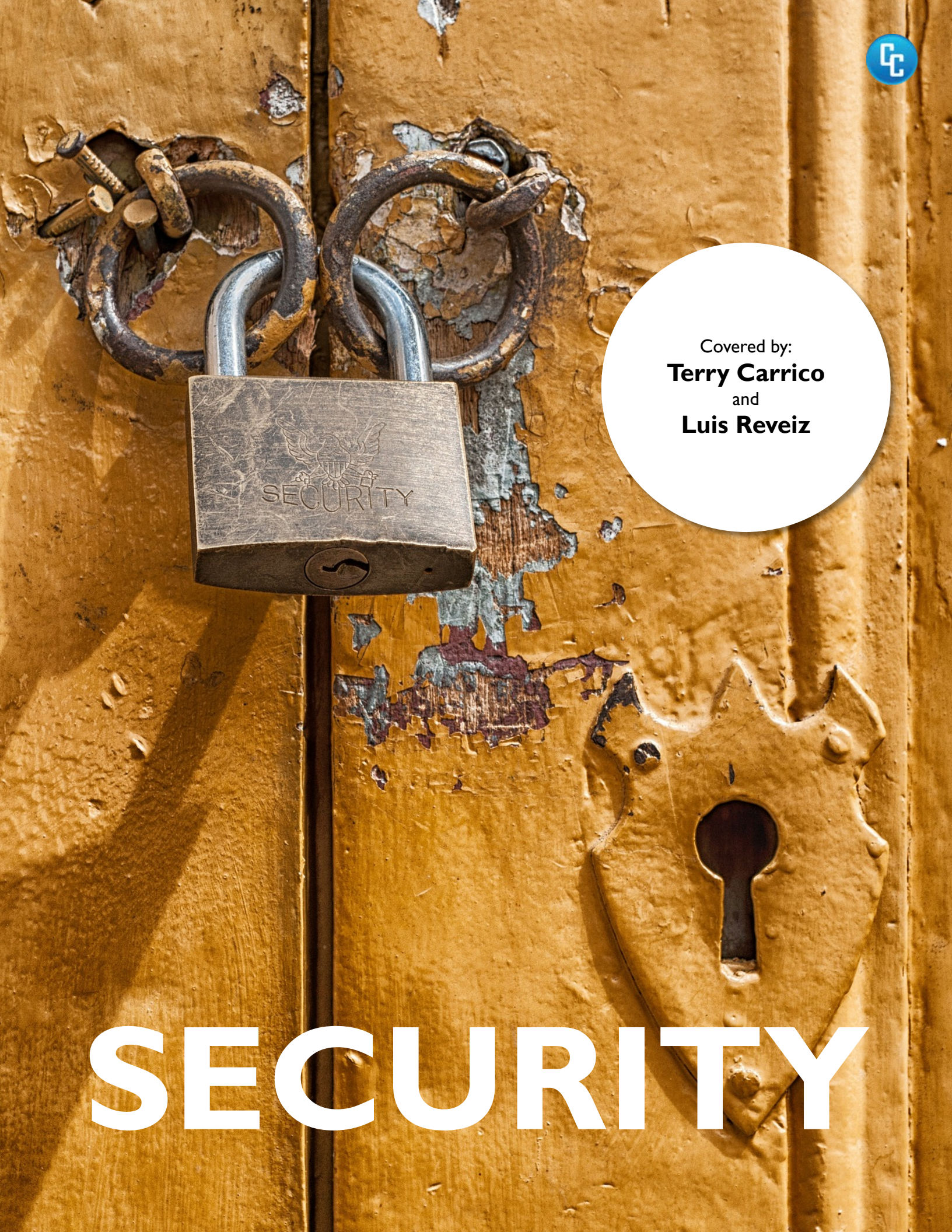
Performance verification over multiple season takes longer than execution of 3 consecutive / concurrent shipments for a TPQ (Transport Performance Qualification).

2

As a result of going over multiple seasons, reports are not always available at time of regulatory inspection.

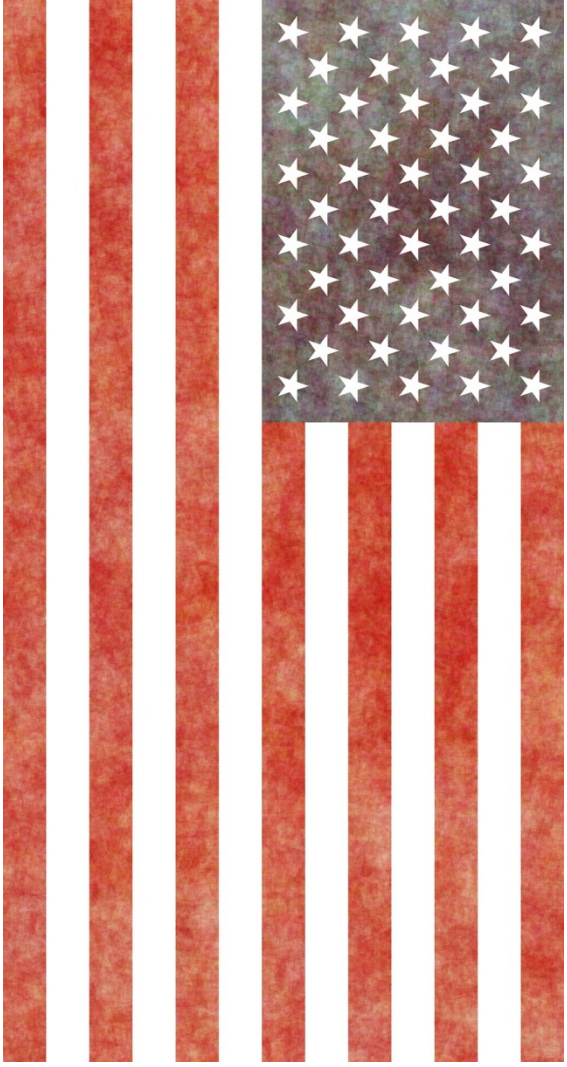
3

Execution of the performance verification is not a centralized activity and relies heavily on resources at the sites and regional levels.



Covered by:
Terry Carrico
and
Luis Reveiz

SECURITY



TERRY CARRICO

VP, Corporate Security and Safety -

McKesson

Terry is responsible for leading all aspects of security operations, including program development in the areas of security standards, physical security, electronic security, supply chain security, employee security awareness, and workplace violence prevention. Prior to joining McKesson in 2007, Terry was employed by Pfizer as Director, Global Asset Protection. In 2003 he retired from the U.S. Army Military Police Corps as a Colonel after serving 24 years. He holds a BS in Criminal Justice and an MS in Forensic Science.

LUIS REVEIZ

Head Global Security –

LatAm Novartis

Luis Reveiz is a former Federal Bureau of Investigations (FBI) special agent and obtained his bachelor's degree from Carson Newman University in 1988. Currently he is the Head of Corporate Security LATAM, accountable for protecting Novartis Group's human, intellectual and physical assets in the region. He leads a multi-talented team that provides a wide range of risk mitigation services to all associates in an emerging market region affected by public insecurity. Luis has 25 years of experience in corporate and government security.

How can companies exert more control over the security practices of their carriers, as well as third parties?

By specifying what's expected in the service contract! A company's security requirements should be included in the contract, and if not adhered to, there needs to be agreed upon consequences for noncompliance. The second most important practice is auditing a carrier's performance, thus ensuring the carrier is adhering to the requirements specified in the contract and thirdly, reward good carrier performance.

Set high level KPI's and hold providers contractually accountable for complying with established security measures financially penalized for non-compliance. Your internal RMP should have a checks and balance system in place that is monitored by your local security teams.

Are there effective theft-prevention measures which could be applied to a given company's supply and cold chains regardless of the situation on the ground?

The implementation of protective measures is not a "one size" fits all, every company must complete a detailed risk analysis of their supply and cold chains to determine the most effective protective measures to deploy. However, there are some fundamental measures that every company should take…it starts with vetting the best carriers to transport your products, and selecting those that adhere to the four pillars of transportation security: preparation, red zone, stops and delivery. The action related to the four pillars of trans security should be the foundational supports for every companies supply chain security program.

How have you managed to keep cargo theft incidents to a minimum in two of statistically worst regions for cargo theft worldwide (Mexico and Brazil)?

The key ingredient is "Duty of Care." This requires hands on involvement from our security teams in both countries, collaborations with key functions within our company, proper due diligence and mandated procedures for our providers that form part of the contractual agreements.

At the summit, you will discuss the mitigation of last-mile threats. Without giving too much away, what are some of the key strategies you've employed to strengthen last-mile security?

A key element of every strategy is understanding the threat(s) and having a plan. One of the most important elements in every company's plan should be delivery driver training. If a driver understands the threat(s), the threat's modus operandi, and remains focused on the task at hand when making deliveries, they can prevent many last mile thefts. There are many other procedural and protective measures that can be used to mitigate or eliminate the threat's impact on your last mile deliveries, which will be shared during my presentation at the forum.

What are some of your strategies to keep security costs low?

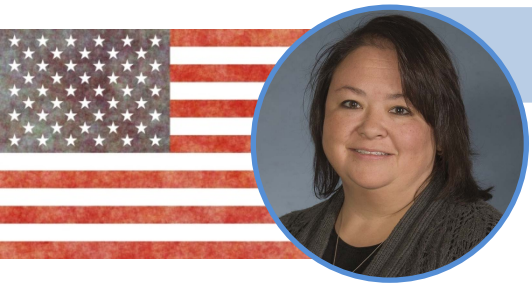
A key factor was to have our local security managers scrutinize and negotiate security charges that were imposed to our logistic groups from transportation and warehouse providers. In most cases these charges were over inflated but accepted as cost of doing business from logistic associates that were not security professionals. The other key to developing effective cost savings is to constantly search for new and more effective security technology that can be incorporated into your Risk Management Program (RMP) that will create savings and subsequently lower insurance premium.

Click on the speaker to find out about their session!

Ropah Hove

Director Pharmacy Services - **Ministry of Health & Child Care, Zimbabwe**

Monitoring the storage conditions for vaccines at health facilities. Evaluation of the quality of product stability data and the conditions under which they were generated.



Lisa Baker

Supply Chain Director - **Amgen**

There is more focus on ensuring the controlled temperature solutions used in shipping specifically meet the needs of the shipping lanes and product requirements. Truly understanding your lanes through proper lane assessments and lane characterization is key for identifying fit for purpose solutions. For the next five years, focus on having robust but cost effective (not over-designing) solutions to ensure cold chain reliability. Data Analytics will be key area to develop as it supports development of the fit for purpose solutions and supports measurement of effectiveness and performance.

Luis Reveiz

Head of Global Security – **LATAM Novartis**

Technology has played a key role in securing the supply chain in recent years and I expect that in the next five years technology can only get better, however we cannot leave out the human and intelligence factor from a robust RMP.

Terry Carrico

VP, Corporate Security and Safety - **McKesson**

Cargo theft is a 15 to 30 billion dollar a year business and it is here to stay. The commodity targets may change, the regional “hot spots” may change but the criminals will continue to target “soft spots” in our supply chains to achieve their objectives. As we have hardened our supply chains making it more difficult for the criminal to succeed, they have become more sophisticated in their schemes, and in the last mile segment more violent, using weapons more frequently to hijack delivery vehicles. In the next five years cargo theft will continue to flourish…making it extremely important for companies to develop and implement protective strategies.

Dana Dallas

Cold Chain Program Manager - **Defense Logistics Agency**

I think the industry has gotten very good at managing the cold chain for refrigerated materials...but I also think they are starting to see that excursions are more common than they think, and in many cases, somewhat avoidable. I have seen a very positive shift in the importance and use of stability data as part of their standard processes vs. the taboo topic that it used to be.

Bernard McGarvey

Sr. Engineering Advisor - **Eli Lilly & Company**

What I hope is that design and optimization will evolve as it would any other engineered system. The role of simulation will increase – vendors already do some of this but there is limited sharing of the output with the customer.

The performance curve approach can help the vendor share a high level view of how the container works without having to share details about what they would consider IP – thermal properties of their PCMs for example. In the long term, this will improve the decision making between the customer and the vendor and this is a win/win for both.

I hope there will be more clarity on how much customers will get involved themselves in simulating containers versus letting the vendor do it all. It may make sense for customers to have some simulation capability but how much remains to be seen.

This process also allows the customer to have a means to understand the performance capabilities of each solution rather than just accepting that the container maintained temps within the acceptance criteria of the say scope document….for example, acceptance criteria says to maintain between 2-8 °C. Vendor designs solution and it maintains between 4-6 °C.

Customer has a means to ask the vendor to optimize to reduce cost complexity etc. to more closely align with better temp performance close to to 2-8 °C. It can also be used in reverse…if too close to 2 or 8 °C, then customer could ask to design to allow more of a tolerance or guard banding.

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