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Managing Unique Temperature Control Requirements

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Biography

- Temperature controlled packaging practitioner
- Consultant to the lifesciences industries
- Package testing and quality systems expertise
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Agenda

- Unique requirements facing brand owners, logistics firms, thermal and supply chain solution providers
- Regulations and Guidance
- Effective solutions implementation for unique requirements

- Cryogenic temperature maintenance
- Supply chain security
- Real time tracking and data response
- Process qualification requirements
- Distribution hazards
- Long distance shipments

Unique requirements facing brand owners, logistics services firms and thermal solution providers

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Cryogenic temperature maintenance

Cryogenic temperature maintenance

What is it?	Hazards	Challenges to brand owners and solution providers	Regulations	Solutions Implementation
Shipping at temperatures below (-) 150°C using liquid nitrogen vapor in a contained system **Dewars**-type of vacuum flask used for storing cryogens (such as liquid nitrogen or liquid helium), walls constructed from two or more layers, with a high vacuum maintained between the layers. This provides very good thermal insulation Driven by development in cell-based immuno- therapies "Giving patients a living drug" T cells	• **Dewars**-High pressure relief of dewars-explosions • Human tissue exposure • Asphyxiation	• Initial qualification • Requalification prior to re-use	US DOT 49 CFR IATA Dangerous Goods UN1977-regulates cargo that contains liquid nitrogen IATA special provision A152– Cryoport *dry nitrogen* (gaseous) shippers--**non hazardous**—liquid nitrogen fully absorbed, pressure not built up, liquid nitrogen not permitted to escape, gaseous nitrogen	• Partnership with solution provider with technology expertise • Data driven 

Supply Chain Security

Supply Chain Security

What is it?	Challenges to brand owners and solution providers	Regulations	Solutions Implementation
Ensuring data provenance—for example cold chain–temperature monitoring Data Provenance is the field of recording the history of data, throughout the stages of the data lifecycle.	• Maintenance of chain of custody • Securing fragmented data—transfer and immutability • Fragmented supply chain ecosystem • Traditional solutions are hosted in private databases—tied to a specific supplier of the service	Drug Supply Chain Security Act—Nov 2013 and Nov 2017 update. Unique product identifier—Fed requirements for drug serialization, transaction documentation (chain of custody) and verification. Nov 2017 update: delay in enforcement of requirement to apply the DSCSA product identifier on drug pkgs and homogeneous cases.	• Partnership with solution provider with technology expertise • Solutions that can integrate with any ERP system • Focus needs to be on data chain of custody • New technologies using IoT and blockchain technology • Blockchain technology is a distributed de-centralized immutable ledger. A shared/semi-shared/private (i.e. permissioned or non-permissioned in the blockchain parlance), **immutable** ledger for recording transactions. Result: high level of trust, accountability, and transparency.

Real Time Tracking and Data Response

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Real Time Tracking and Data Response

What is it?	Challenges to brand owners and solution providers	Regulations	Solutions Implementation

• "Real-time" data is **more actionable** than "track and trace" data:
• **Awareness of an issue**: If you know that your temperature is rising in real time, you can take immediate action to mitigate the risk.
• **Reduced reaction time to fixing a problem**– thereby increasing the probability of successfully fixing it.
• **Action insights:** You will also know in real-time if the problem has been fixed and the temperature is once again within the established thresholds.
	• What is the frequency at which I need visibility data?
	• Do I need only current data or also the past-data audit trail?
	• What parameters are critical to monitor?
	• real-time location, temperature, atmospheric pressure, humidity
	• What is the level of visibility I need? At a vehicle, container, pallet or shipment level?
	• Action plan (response) for real time data collection—understand what data you are collecting and the implications of data variability– Frankenstein data—**Define action response for data limits**
		• ICH "**Guidance** for Industry"--stability testing-proper management of temp excursions in shipping and short term storage applications.
		• EU Guide to Good Manufacturing Practice, Annex 13
		• Guidelines on Good Distribution Practice of Medicinal Products
		• CDC Guidelines for Maintaining and Managing the Vaccine Cold Chain
		• WHO Guidelines
		• PDA Technical Report 39
		• US Code Fed Regulations
		• US and EU Pharmocopoeia
			• A network of cross functional stakeholders
			• Launch execution
			  • Shipping risk mitigation
			  • Pack out solutions for clinical trials, testing, global distribution
			  • Real time tracking solutions, **rapid problem solving**
			  • **Performance history**—value of data collection **"big data"**—predictive, modeling"
			  • **Reverse logistics**, "after market"--monitor for counterfeit and/or diverted product, expired product and trade returns. Options that include **authentication** of product in the field and during the reverse distribution cycle of the supply chain.

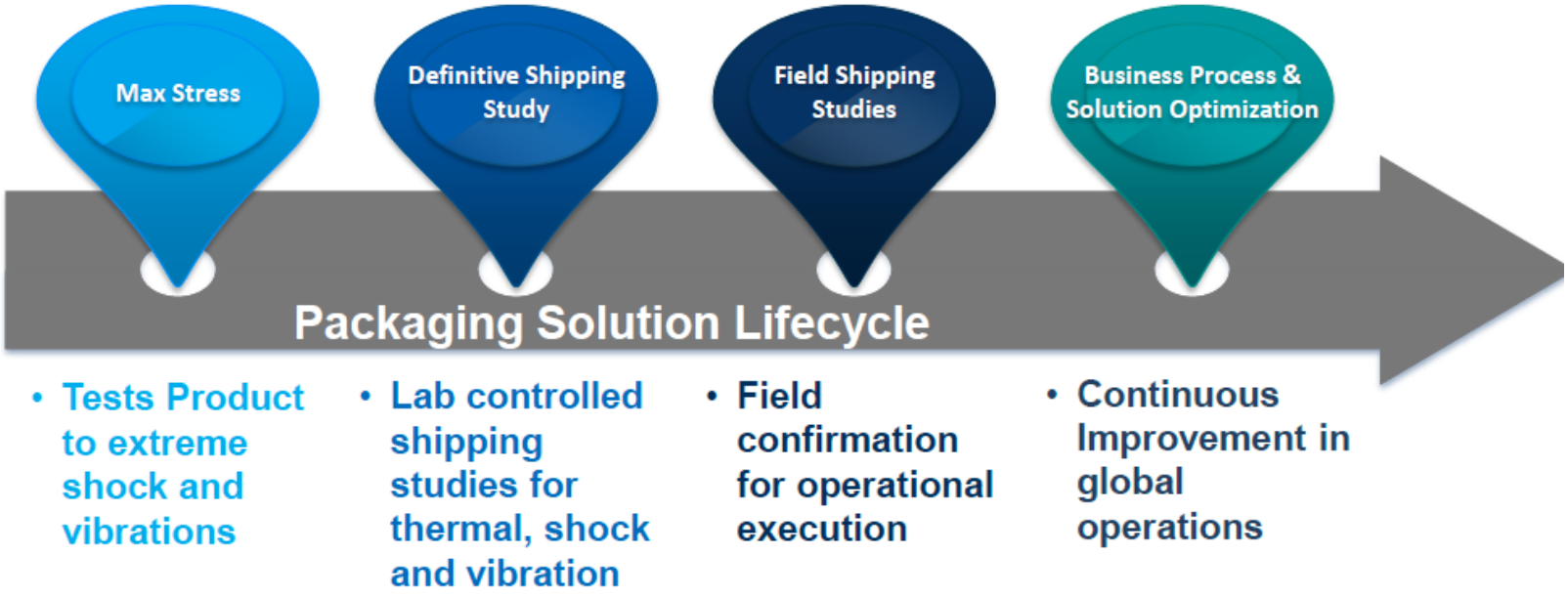
Process Qualification

Process Qualification

What is it?	Challenges to brand owners and solution providers	Regulations	Solutions Implementation

Process qualification: The collection and evaluation of data, from the process design stage through commercial production, that establishes scientific evidence that a process is capable of consistently delivering quality products.	• Initial qualification of the thermal packaging process—end to end:
	  • thermal packaging performance qualification
	  • Pack out documentation
	  • Actual Shipping/distribution performance testing
	• Re-usable systems:
	  • Requalification prior to re-use
		•FDA Guidance for Industry: Process Validation, General Principles and Practice, cGmp Jan 2011	•Cross functional teams
			•Quality systems
			•Risk management approach
			•Detailed supply chain logistics information
			•Gap analysis with the end state in mind:
			  • to include regulations compliance, risk assessments, supply agreements
			•***Packaging solution lifecycle***—*Eli Lilly, Michael Broughton*
			•IQ, OQ, PQ –surveillance program for re-usable, every year or mid point of life
			•Real world performance qualification
			•DQ of shipper vs profile-ISTA 7E, ASTM D3103
			•Active monitoring of shippers
			•Data gathering vs. acceptance criteria—critical to define action response to data limits. Qualify data conditions and action response.

Process Qualification



Attribution: Eli Lilly, Michael Broughton, September 2017

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Distribution Hazards

Shock
Vibration
Temperature
Humidity
Light sensitivity
Low Pressure, High Altitude

Distribution Hazards

What is it?	Hazards	Challenges to brand owners and solution providers	Regulations	Solutions Implementation

Mechanical and environmental effects encountered during shipping, handling and storage throughout the entire supply chain	• Temperature extremes
	• Humidity extremes
	• Vibration and shock impacts
	• Low pressure (high altitude)
	• Light sensitivities
		• Defining, evaluating and modeling the extremes
		• Thermal shipper design solutions to effectively meet design requirements
		• **Time to market**—
		  • Design requirements
		  • Design time including iteration
		  • Effective and timely qualification protocols, Considerations of pallet load, single parcel designs for qualification
			Guidance for Industry-Container Closure Systems for Packaging Human Drugs and Biologics—*Performance–evaluation of suitability-functionality and drug delivery*	• Performance qualification protocol development, PQ
				• Typically a core competency of a packaging engineering professional
				  • Distribution protocol development—either ASTM D4169 or ISTA 3A or 3H, 3-series
				  • Define pallet load and single parcel shipments
				  • Determine if high altitude low pressure has effects on primary and shipping containers

Long Distance Shipments

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Long Distance Shipments

What is it?	Hazards	Challenges to brand owners and solution providers	Regulations	Solutions Implementation

Global distribution	• Same as distribution hazards
	• Ocean shipments are becoming more common for cost effectiveness
		• Environmental hazards
		• Customs and logistics challenges!
		• Multiple transport modes-sea, air, land—challenge of laboratory simulation
		  • Containerized cargo(seatainers) for ocean transport
		  • 45 day ocean voyage-one way!
		  • Environmental extremes of high humidity and elevated temperatures
			Import/Export regulations-country specific	• Performance qualification protocol development, PQ
				• Typically a core competency of a packaging engineering professional—caveat—ocean shipment knowledge, not widespread competency
				• Distribution protocol development—either ASTM D4169 or ISTA 3A or 3H, 3-series

Strategies for Success

- Value in partnering with solutions providers with the requisite expertise
- Prioritize Goals:
  - Patient safety
  - Compliance
  - Business process excellence
- Start with the end state in mind:
  - Unique requirement—e.g. convert 25% of air shipments to ocean shipments with zero excursions for temperature
- Gap Analyses—understand current state vs. goal
- Execution success--create a clear vision

Thank you!

Questions?

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