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Welcome



Empowering a healthy tomorrow

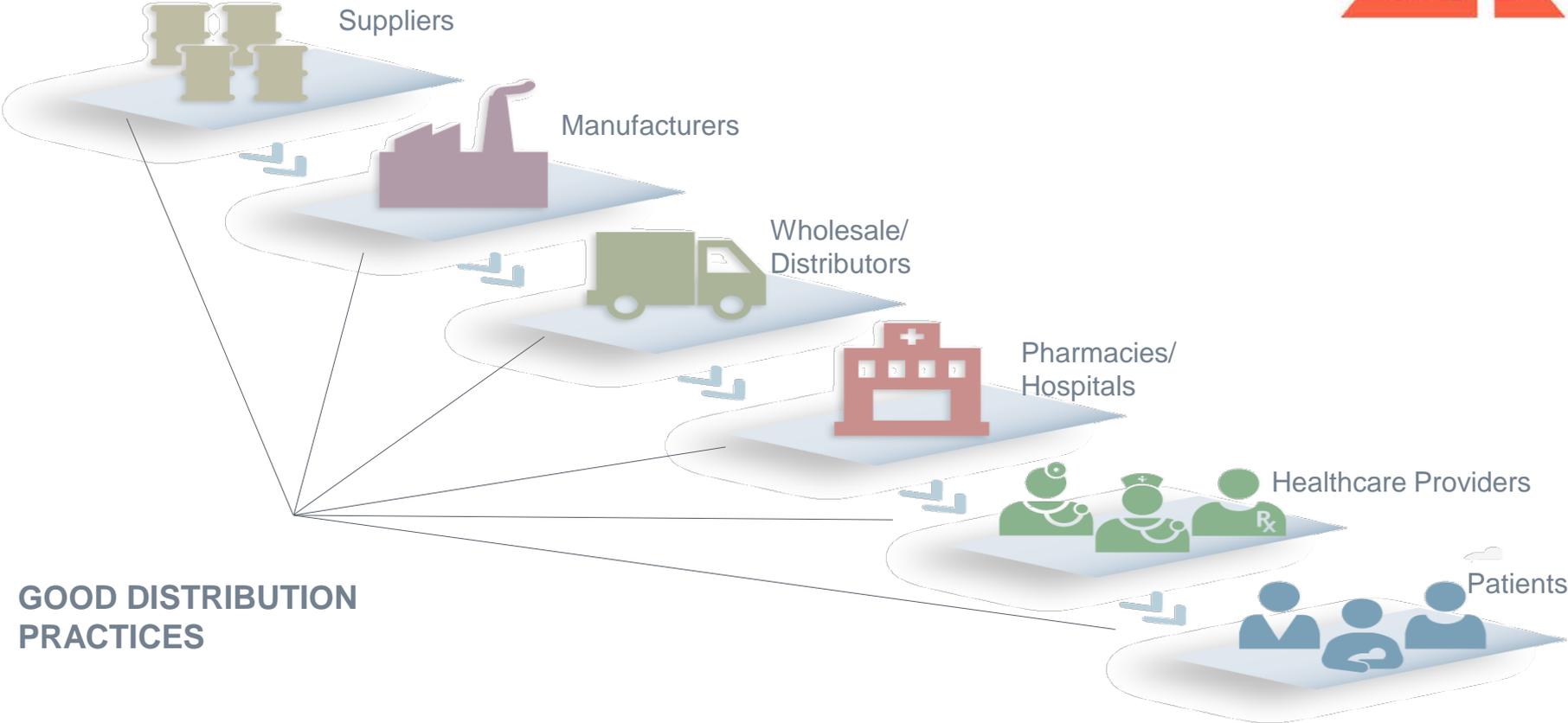


<659> Packaging and Storage Requirements and <1079> Good Storage and Distribution Practices: Highlights

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Good Distribution Practice



GOOD DISTRIBUTION PRACTICES

The Old View



- A Manufacturer's responsibility ended at its loading dock...



<659> Packaging and Storage Requirements



- Every monograph in USP-NF must have packaging & storage requirements
- <659> provides the choice of containers
- Official 1 May 2019: dosing cups, spoons, oral syringes, etc. must be marked in metric units corresponding to the dosing instructions

Which one is a teaspoon?



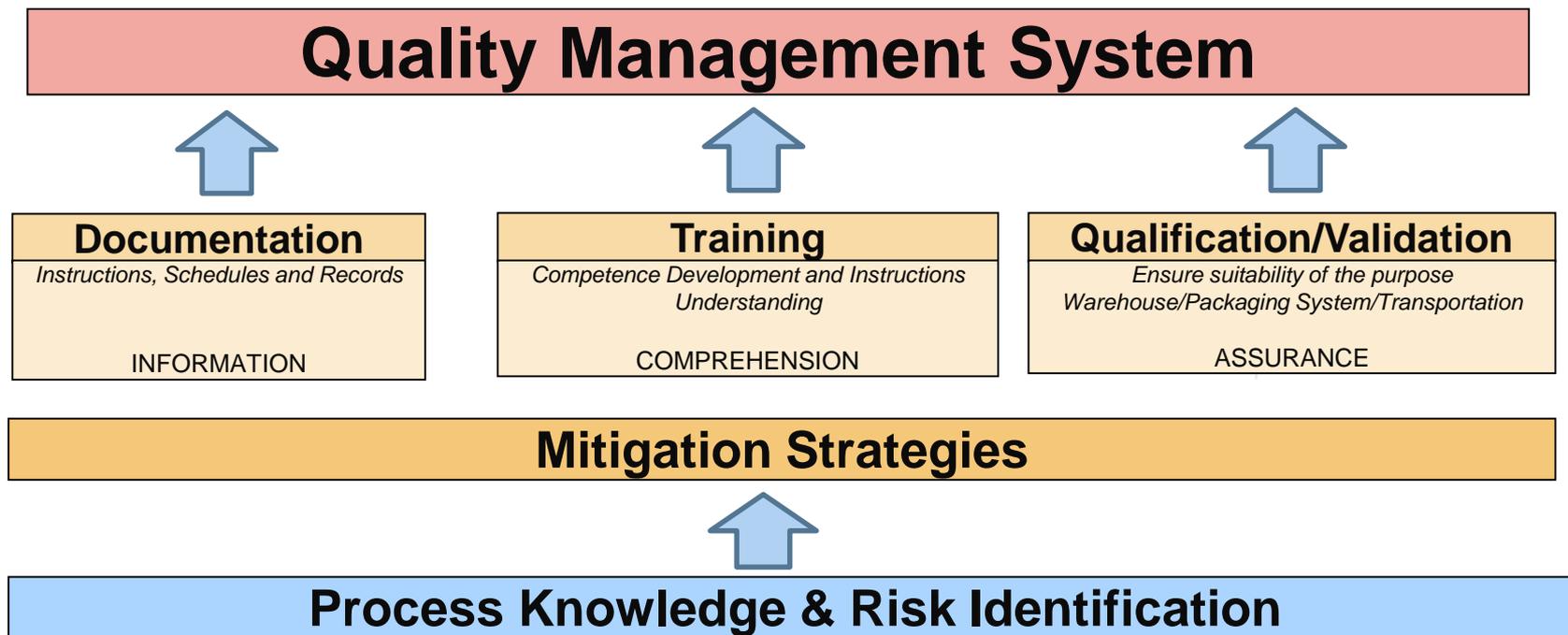
<1079> Good Storage and Distribution Practices



<1079> Good Storage and Distribution Practices (*Official*)

- ▶ Future Focus
 - **Storage and Transportation** of Finished Drug Products
 - All organizations and individuals involved in the storage and transportation of drug products
 - Risk-Based Approach to the Storage and Transportation of Drug Products
 - Risk Identification
 - Mitigation Strategies

Risk-based Approach to Storage and Transportation



The central idea is having a Quality System that is build based on risk. Generally, mitigation strategies are related to instructions (SOPs), training (ensure instructions understanding) and Qualification/Validation (warehouse temp map, packaging system, ERP software, process validation (in case of distribution, is the transport mode/route validation).

And all of this are GDP requirements!



- ▶ **Product and process knowledge is the starting point in identifying risks related to the storage and transportation.**
 - Product knowledge:
 - Intended use
 - Storage conditions
 - Potential hazards from the material (to environment and personnel: e.g. hormones, cytotoxic drug products, radiopharmaceuticals, etc.)
 - Potential hazards to the material (e.g. stability, high potential of abuse; high value drugs; attractiveness for cargo theft, counterfeiting, diversion).
 - Process knowledge:
 - Knowledge of supply chain partners
 - Physical modes of transportation (air, sea, rail, or road)
 - Transportation routes



- ▶ **Risk identification is the systematic use of information to identify potential sources of harm (hazards).**
 - Information can include historical data, theoretical analysis, informed opinions, product and process knowledge and the concerns of stakeholders.
 - Risk identification addresses the “what might go wrong?” question.



- ▶ **Mitigation strategies seek to limit or avoid the identified risks through:**
 - Documentation: instructions for a specific operation or process in order to standardize and establish consistency
 - Training: ensuring instructions are understood
 - Resources: having capability through infrastructure and human resources (infrastructure and human)
 - Qualification/Validation: the assurance that the resources and processes are reliable, reproducible and robust.



- ▶ **Key documents that are fundamental for a QMS that supply chain partners can implement in their organizations:**
 - Quality Manual
 - Standard Operating Procedures (SOPs)
 - Labels
 - Receiving
 - Storage and Transportation
 - Supplier Qualification
 - Quality Agreements
 - Recalls
 - Returns
 - Excursion Handling



- ▶ Training is a critical process to communicate job expectations and to develop skills to effectively and efficiently execute daily responsibilities.
 - Training should be covered in a training SOP
 - Training may be:
 - Instruction led by qualified instructors or subject-matter experts
 - On-the-job training by a supervisor or other qualified personnel
 - Web-based training or simulations.
 - Training effectiveness determined



▶ Qualification

- Facilities/equipment
- Thermal packaging and transportation systems
 - Assurance that systems or equipment meet predetermined acceptance criteria before use

▶ Validation

- Process and Procedures
 - Assurance that processes produce the desired outcome

▶ Calibration

- Instruments or device
 - Assurance that they produce results within specified limits



- ▶ **Resources are storage, transportation and personnel.**
 - Storage
 - Premises should be designed to maintain the quality and integrity of drug product stored
 - Transportation
 - All vehicles used in supply chain activities, such as semitrailer trucks, vans, trucks, trains, airplanes, sea vessels, mail delivery vehicles, and emergency medical services, should be suitable for the intended purpose.
 - Personnel

Risks and Mitigation Strategies



HAZARD	EFFECT	MITIGATION STRATEGY	MITIGATION CATEGORY/ AVENUE
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Storage

Improper entry to ERP-like systems: (wrong batch number, wrong expiration date, wrong status e.g. approved product that should be quarantined); wrong amount)	<p>Cannot have an accurate information of the stock</p> <p>Can pick and ship a product that was supposed to be quarantined but due to wrong status was marked as approved</p>	<p>Stocking SOP</p> <p>Software validation</p>	Documentation and Validation
Product has been stored in the wrong physical location	<p>Picking issue mistakes (software will show the location however you can pick the wrong product if there is no check of physical placement)</p> <p>Product can face excursions</p> <p>Legal sanctions for Controlled Substance Risk of diversion for Controlled Substance</p>	<p>Stocking SOP</p> <p>Automated checking system</p> <p>SOP that shows a list of products and their Temperature Specification</p> <p>SOP that shows a list of products and their license category (controlled, radiopharmaceuticals, etc.)</p>	<p>Documentation and Validation</p> <p>Documentation</p> <p>Documentation</p>

Risks and Mitigation Strategies



HAZARD	EFFECT	MITIGATION STRATEGY	MITIGATION CATEGORY/ AVENUE
Storage			
Environmental conditions out of specification	Affects product quality, integrity and patient safety (e.g. freezing of vaccine or biologic) Product loss (e.g. money)	Warehouse, packaging and transportation qualification (temperature mapping) Product storage identification	Qualification/Validation Documentation
Temperature Monitoring Device Failure	Out-of-range cold or hot areas; Product storage temperature excursion; Product loss	Back-up monitoring devices with independent power source Excursion handling SOP	Documentation/Resources
Storage /Temperature System Failure due to: loss of electrical power failure of temperature control and air circulation systems unusual weather event	Out-of-range cold or hot areas; Product storage temperature excursion; Product loss	Temperature and power alarms, Back-up power and coolant systems (redundant) and/or contingency storage; Excursion handling SOP	Documentation/Resources

Risks and Mitigation Strategies



HAZARD	EFFECT	MITIGATION STRATEGY	MITIGATION CATEGORY/ AVENUE
Receiving/Shipping			
Receive an adulterated, falsified, recalled product	Introduction into legitimate supply chain a product that is potentially substandard, illegal or counterfeited	Quarantine Quality Control test Packaging identification fingerprints Recall awareness Notify regulatory authorities or trading partners	Documentation
Receive some product that was not ordered	Unmatched transaction (e.g. wrong paper work/transaction data sent) Introduction into legitimate supply chain a product that is potentially substandard, illegal or counterfeited	Receiving SOP and training	Documentation and Training

Risks and Mitigation Strategies



HAZARD	EFFECT	MITIGATION STRATEGY	MITIGATION CATEGORY/ AVENUE
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Receiving/Shipping

<p>Mix-up products with different status (Rejected/Recalled/Returned)</p>	<p>Shipping/selling of inappropriate product</p>	<p>Product segregation</p> <p>Warehouse layout (logical flow and holding areas in order to avoid mix ups)</p> <p>Receiving SOP</p>	<p>Documentation and Resources</p>
<p>Shipping/Receiving delays due to inclement weather, natural disasters, traffic disruption</p>	<p>Arrival delays</p> <p>Temperature out of specification (Temperature excursions, e.g. accidentally freezing when is snowing)</p>	<p>Reschedule the delivery</p> <p>Temporary parking (waiting for availability to unload). This could mean offloading to temperature controlled facility or vehicle</p> <p>Recondition materials to ensure temperature maintenance during delay</p> <p>Rescue Services</p>	<p>Documentation</p>

Control Cold Temperature Definition



- ▶ First Supplement USP 29
- ▶ General Notices: Section 10.10 – Preservation, Packaging Storage and Labeling
- ▶ Official April 1, 2006
 - Controlled Cold Temperature — This temperature is defined as the temperature maintained thermostatically between 2 and 8° (36 and 46 F), **that allows for excursions in temperature between 0 and 15 ° (32 and 59 F)** that may be experienced during storage, shipping, and distribution such that the allowable calculated MKT is not more than 8 ° (46 F). Transient spikes up to 25 ° (77 F) may be permitted if the manufacturer so instructs and provided that such spikes do not exceed 24 hours for cold storage.
- ▶ Definition was omitted in USP 37 in 2013, because excursions down to 0°, could not be scientifically supported
- ▶ PD EC to propose another definition for Control Cold Temperature in <659> in PF 44 (4) July, 2018

- ▶ Stimuli Article : PF 44 (4) July 2018
 - **The Use of Mean Kinetic Temperature to Aid Evaluation of Temperature Excursions: Proper and Improper Application**
 - Describes the use of mean kinetic temperature (MKT) to evaluate temperature excursions for shipments of controlled room temperature (CRT) and controlled cold temperature pharmaceutical products. Correct and incorrect uses of MKT are described and supported by examples from actual events. Authors will propose using 30 days to calculate MKT for CRT and 24 hours for controlled cold temperature products, including excursion time.
 - ▶ objectives of article are to initiate discussion and solicit public comments regarding the new USP position on how to use MKT to evaluate temperature excursions of pharmaceutical drugs

Conclusion



- ▶ Product and process knowledge is the starting point in identifying risks related to the storage and transportation
- ▶ The mitigation strategies should be put in place to off set the risk related to storage and transportation
- ▶ The mitigation strategies can be divided into four essentials pillars:
 - Documentation
 - Training
 - Qualification/Validation
 - Resources
- ▶ Identifying storage and transportation risk and putting in place the appropriate mitigation strategies will enhance quality assured processes, maintain product quality and supply chain integrity.

Thank You



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Your partner in
accelerating
life science product
development

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