PHARMACEUTICAL COMMERCE

TRAINING TO MEET TEMPERATURE-CONTROLLED LOGISTICS CHALLENGES

Manufacturers must go beyond technology solutions to meet regulatory requirements

Not too long ago, it was commonly thought that the logistics aspect of the FDA-regulated pharmaceutical supply chain was a fairly insignificant aspect of the industry's in-depth research to market cycle. Today, that mindset has come full circle and we continue to move to a stronger sense of partnership encompassing the logistics service providers and pharmaceuticals manufacturer. What closed the gap? Education.

A typical U.S. company spends more than $1.5 million annually on internal employee training. Seventy percent of companies also report training as one of their top five key initiatives, recognizing that training done well can increase efficiencies and improve customer satisfaction resulting in better profits. In global pharmaceutical market, training takes on an even greater scope as you add layers of ever changing regulations, varying interpretations of those regulations, and the reliance of outside providers such as logistics companies to support your needs.

Pharmaceutical companies may find that their internal training procedures fall short once they hand over the reins to their service providers. You no longer have a captive audience or a singular communications vehicle. Ensuring the latest standard operating procedures are reviewed and understood across different organizations who may speak different languages may seem a near impossibility. A hazardous material, "poison," label in the U.S. looks an awful lot like, "poisson;" in French, meaning fish. The way one transports fish is far different than the way one should handle a poisonous material.

Improving efficiencies, complying with regulations, developing solid partnerships and increasing your bottom line all start with education. Education begins with understanding all facets of your drugs' life cycle and identifying who will be a part of each step, what type of impact they may have on your drug and then, of course, the ultimate risks and rewards each participant may affect. The critical piece of this is to then trust in your service partners and share the areas of risk and concern. Only then will they have the foundational education needed to develop the right solutions, robust contingency plans and mitigate risk.

Implement a Due Diligence Plan

	Prior to Shipping	During Transit	Hand Offs	Delivery
All	• Training • Quality Agreements • Audit & approvals	• Monitoring • Contingency • Documentation	• Responsibility	• Receipt • Approval • Movement to controlled storage
Ground	• Vehicle is preconditioned • Confirm & Document prior movement & handling • Confirm label requirements	• Real-time monitoring • Alarms • Control	• Dropped trailer visibility • Cross dock temperatures	• Audit Trail documentation provided
Air	• Container management • Booked space • Alternate routes – flights identified	• Dry Ice locations • Repack solutions • Monitoring capabilities	• Defined procedures from aircraft to sort/truck • Airport provide controlled storage	• Same as above
A Product out of Temperature Control = An Adulterated Product				

Global Consistency for Temperature Sensitive Products

	WHO	USP	Health Canada	FDA
Good Manufacturing Practices Apply	Yes	Yes	Yes	Yes
Monitoring Required	Yes- No Guidelines on How Often	Yes- No Guidelines on How Often	Yes- No Guidelines on How Often	Yes- No Guidelines on How Often
Vehicle Mapping Required	Yes	Yes- Recommend	Yes- if used as primary mean of environmental control	Yes
Written Procedures Required	Yes	Yes	Yes	Yes
Global Consistency Allows for Unified Procedures Increasing Efficiencies				

Labeling requirements

The poison and fish example may seem unlikely but, let's look at the guidance and regulations around labeling. The FDA regulates labeling operations within Code of Federal Regulations (CFR) Title 21, section 211.13 which states, "There shall be written procedures designed to assure that correct labels, labeling, and packaging materials are used for drug products; such written procedures shall be followed." Furthermore, "these procedures shall ensure the prevention of mix ups and cross-contamination by physical or spatial separation from operations on other drug products."

As a logistics provider, I need to understand what the labels are meant to communicate so that the average person (read: truck driver or material handler) can make the right decisions while pharmaceuticals products are in our control. The very controlled world of pharmaceutical manufacturing is almost polar opposite of the variability (climate, weather, traffic, mechanical failures etc.) found in transportation. Education and communication are keys to closing that gap.

Labels are great but not if they can't be read or understood

- Ensure that when placing product boxes onto skids for shipping that the labels can be read from all sides, even after shrinkwrapped.
- When loading product into secondary shipping containers, ensure that the labels can easily be read by opening the cargo door.
- When loading shipping containers with temperature readouts into a truck ensure that the readouts face out so that they can be easily monitored.
- If your products storage label reads 2-8C but your shipping outside of that, say 0-15°C, ensure that your shipping paperwork is clear, maybe "OK to ship outside label requirements at 0-15°C."

Contingency plans, details count

- All dry ice is not the same. If your logistics plans require a re-ice of a shipping container, ensure the right calculations are used. There's a difference between how quickly blocked vs. pellet dry

ice dissipates.
- Knowing the hazardous materials requirements of dry ice handling and disposal for each point in your logistics chain can be critical.
- Qualifying refrigerated trailers to include a power failure can be key when trying to implement the right plan if equipment breaks down.

Quality Agreement and SOP's – Know who's going to do what and how

- Monitoring of product is recommended in some countries and required in others. Ensure that the methods of documentation are acceptable and practical.
- Deviation reporting should be defined. No one wants to be inundated with data that is not necessary but often there's a fine line between don't need and critical.
- Manufacturers hold all the responsibility in the eye of the FDA. But, responsibility for properly managing pharmaceuticals in the supply chain lies with your logistics partners.

Just like in any investment, you only see a solid return if you enter into the relationship with an understanding of risk and a plan to mitigate. Education and communications are the keys to a solid relationship between pharmaceutical manufacturers and the service providers entrusted with the transportation of their products.

So what happens if a manufacturer misses the target on the education landscape internally and with their logistics service providers? Training is a clear component of the Quality System Regulation found in Title 21, Code of Federal Regulations Part 820.

Failure to comply with the aspect of current Good Manufacturing Practice can be costly. The FDA listing of recent 483 warning letters details the significant ramifications clearly. For example, in a citing issued from last July, FDA inspectors made the following findings within an organization. Excerpts of that finding include:

Violations of the Quality System Regulation
This inspection further revealed that these devices are adulterated within the meaning of Section 501(h) of the Act [21 U .S.C. 351(h)], in that the methods used in, or the facilities or controls used for, their manufacture, packing, storage, or installation are not in conformity with the current Good Manufacturing Practice (cGMP) requirements of the Quality System (QS) regulation found at Title 21, Code of Federal Regulations (CFR), Part 820.

Failure to establish and maintain procedures for implementing corrective and preventive action, including requirements for identifying the action(s) needed to correct and prevent recurrence of nonconforming product and other quality problems, and requirements for implementing and recording changes in methods and procedures needed to correct and prevent identified quality problems, as required by 21 CFR 820.100(a)(3) and 820.1 00(a)(5) .

Failure to establish and maintain procedures to ensure that all purchased or otherwise received product and services conform to specified requirements, failure to evaluate and select potential suppliers, contractors, and consultants on the basis of their ability to meet specified requirements and failure to document the evaluation, as required by 21 CFR 820.50(a)(1) .

Failure to ensure that all personnel are trained to adequately perform their assigned responsibilities and to document the training, as required by 21 CFR 820.25(b).

It's clear in the above finding that the FDA expects that manufacturers include the suppliers and vendors in their CAPA programs. Training, education and monitoring of supplier and vendor activities are crucial for compliance to FDA regulations. Inability to meet these regulations may end like this example with warnings of seizure or monetary penalties.

In another recent 483 Warning Letter, filed in August 2008, the FDA finds the drug manufacturer is deficient in more than 20 areas including the following finding addressing written procedures regarding labeling products:

There are no written procedures describing in detail the receipt, identification, storage, handling, sampling, examination, and/or testing of labeling and packaging materials [21 CFR§ 211 .122(a)] . For instance, your firm has no written procedures covering the receipt, examination, storage, and handling of labeling and packaging materials used to produce the finished drug products.

Logistics providers may be able to help to prevent finding such as the one highlighted here. With clear communications and identification of the types of materials service providers transport, written procedures can easily be established that aid in describing requirements for receipt of products, product labels and packaging. Turning to you service provider to help establish requirements and detailing the expectation and need for documentation of the events supporting the procedures addresses two of the findings above. It helps document written guidelines for the qualification of service providers, as well as, establishes a documented audit trail for the receipt, storage and handling of products.

Logistics providers want to be your partners. And, we embrace the idea of written procedures teamed with the tools of knowledge and education to execute a flawless relationship. It helps us streamline our operations, develop performance benchmarks, identify deficiencies, implement needed corrective and preventative actions and, they allow us to understand our level of risk and liability. It makes us better partners. Logistics transportation has found its way into the 483 Warning Letter world as well, especially for pharmaceuticals requiring temperature controls. PC

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