5 Steps to Reduce Temperature Excursions for Pharmaceutical Products

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Introduction

Many risk factors impact the products that pass through the Pharmaceutical Supply Chain. While these risks can be adequately mitigated, many are out of the shipper's direct control. To experience success when distributing temperature-controlled pharmaceutical products, a firm must first control all aspects of the process within its walls. Then the firm must forge solid working relationships with partners in the supply chain to work together as one cohesive team.

The five steps outlined in this paper can be implemented with minimal effort at little to no cost to the business. Those tasked with the safe transport of temperature-controlled medicinal products must strive to control as much of the supply chain as possible by continuously strengthening relationships with supply chain partners in order to appropriately mitigate potential risks as a team.

Several Parenteral Drug Association (PDA) Technical Reports (TR) have been published as guidance for handling, storage, distribution, and risk mitigation for shipping of temperature-controlled products [1-6]. These complement many of the regulatory requirements that continue to be added such as the New European Union Good Distribution Practice of Medicinal Products for Human Use [7] and the Irish Medicines Board (IMB) Guide to Good Distribution Practice of Medicinal Products for Human Use [8]. The New USP <1083> Good Distribution Practices – Supply Chain Integrity covers the Quality Management System, Environmental Conditions Management, Importation and Exportation Management, and Supply Chain Integrity and Security [9]. Recently, due to theft, tampering, diversion, and counterfeiting of medicinal products, security of the supply chain has received considerable attention. See, for example, the 2014 PDA/FDA Pharmaceutical Supply Chain Conference with Educational Support from Rx – 360 [10]. The convergence of environmental monitoring and supply chain security offers some of the new tools to combat the above mentioned illicit activities [11].

Challenges

There are many challenges in handling, storing, and distributing temperature sensitive pharmaceutical products. Examples of challenges may include but are not limited to:

- Traffic delays
- Weather
- Mechanical failure — cooling systems, vehicle failure (truck and aircraft)
- In transit damage
- Miscommunication
- Customs delays
- Product exposure on tarmac or loading dock

These challenges would result in a rejected or adulterated product that may not be safe or efficacious to use. It is the responsibility of the shipper, along with all supply chain partners, to ensure that such risks are adequately mitigated against.

These risks may be addressed by implementing the following steps:

- Defining and maintaining relationships between supply chain partners
- Ensuring clear communication through the supply chain
- Performing accurate trending and root cause analysis
- Increasing internal knowledge in critical areas
- Evaluating and selecting appropriate packaging

The 5 Steps

The following 5 steps provide a roadmap for implementing simple changes in a shipping program that will result in reduction of days in transit, decrease in excursions, and higher overall rate of performance for both the organization and its partners.

Step 1: Ensure that effective and detailed Quality Agreements are in place with the supply chain partners [12,13]

Quality agreements are not a new instrument by any means, but they have received increased attention as of late [14,15]. There is a current trend in the pharmaceutical industry to bring quality agreements to the forefront of supply chain relationships. It has become increasingly apparent that the quality agreement, while providing some level of accountability, had become a retroactive way to address adverse events, answering questions such as, "Who didn't perform as expected?" "Who will initiate the investigation?" or "Is an event induced audit required?" While these are all important matters that should be addressed within quality agreements, the tool should also be used as a way to circumvent these potential events. Indeed, Quality Agreements are able to serve as a proactive step in controlling the shipping of drug product.

The industry trend for quality agreements serves to provide a more visible document to facilitate strong partnerships between firms in the supply chain. Rather than being a list of expectations for the supply chain vendors, the quality agreement should include accountability for all partners, including manufacturers. The agreement should drive the relationship and provide clear insight into how the partnership will work and what each party can expect from the other. This type of quality agreement should address the responsibilities of all parties in the event that contingency plans need to be implemented. They should also specify what key performance indicators (KPI's) are being tracked on all partners as well as internally, and at what point during trending follow-up conversations will be conducted. Finally, Quality Agreements should include how key information, such as acceptable time out of storage as part of the stability budget, will be shared across partners.

The quality agreement has shifted from being a document that is rarely referenced to one which defines and strengthens the relationship between supply chain partners. The days of having purely transactional relationships with partners have passed, and only those firms that consider the supply chain as a whole as opposed to only their specific facility will succeed in today's pharmaceutical industry. Providing these types of agreements to the service-providing partners will go far toward assessing their true willingness to work together with the firm to provide quality service.

Step 2: Use tools to ensure seamless flow of information between partners

One of the most common causes of temperature excursions for pharmaceutical products is miscommunication. In order for partners in the supply chain to perform together effectively, there must be clear and concise sharing of information and shipment requirements. It is not beneficial for either partner to have complete information internally if that information is not shared downstream.

There are many modes of communication utilized by individual supply chain firms to share information with their partners. Service providers all have their preferred methods of communication, which may include email, web portal, facsimile, or phone calls. All of these types of communication can be used to transfer information downstream to partners when planning for material shipments. The transferred information will then be entered into the service provider's system to capture details of the shipment. While it may be productive to follow the processes of partners as closely as possible and use their preferred method, it is still a good idea to have one standardized way to gather and transfer information that takes precedence over all other entries. One tool that can be used in conjunction with the partner's preferred method is creation of a worksheet containing all the specifications for a particular shipment. The worksheet should contain at a minimum:

- End recipient information
- Shipment reference number
- Shipping solution being utilized (shipper specs, temperature, coolant used, pack out instructions, qualified time, pre- and post-qualification expiration handling instructions)
- Shipment pack out time
- Temperature Monitor details (monitor used, monitor limits, monitor life)
- Product information (dimensions, weight, Hazmat considerations)
- International information (paperwork included, Harmonized Tariff Codes, value)
- Emergency contact information
- Follow up section (issues, delays, delivery date, deviation/ investigation references)

Creating such a tool will ensure that all pertinent information is compiled internally prior to scheduling any material movements. Providing this information to the partners will also guarantee that they have all required information regardless of what is requested using their preferred method of scheduling. This information can be used to trump any old notes possibly saved in the partner's system, or be used as an internal reference for others should the original point of contact for the shipment be unavailable for any reason. The form developed by BioConvergence for this purpose is used primarily for international shipments; however, a modified form can be used for domestic shipments if needed.

Step 3: Track comprehensive metrics/key performance indicators (KPI's) both on the partners and internally to the organization

KPI's and metrics have been used in the pharmaceutical industry for years to evaluate performance and provide feedback to internal personnel as well as service-providing partners. It is essential, though, to ensure the firm is collecting the correct metrics. While the intent of gathering these KPI's is to gauge performance levels, collecting incomplete or incorrect metrics can actually be detrimental to the organization.

An evaluation must be performed to assess which data will be gathered. The key is to ensure that the data do not leave any gaps, or true trending, thus resulting in difficulties for root cause analysis. The metrics should be a comprehensive set of data which accurately reflect the performance of all internal personnel and processes, packaging solutions, and external partners' performance. Omitting but one small piece of the process might be misleading during later evaluation.

For example, when recording the origin, packaging solution, carrier, season, and destination data for shipments and an unfavorable trend emerges, it might mistakenly be attributed to one of those factors when the actual root cause might be operator error in packing out the shipper. Without tracking the operator performing the shipments, one would not observe that the operator was the common denominator in all shipments experiencing excursions. Simply leaving out one variable can result in the wrong direction when performing root cause analysis and might lead to the discontinued use of a product or partner when such action is truly unwarranted.

Detailed metrics can also be extremely useful in determining when to use specific shipping solutions or partners' services. Depending on variables such as seasonality and destination, some solutions may perform better than others. Each individual shipment can utilize a custom grouping of components determined by reviewing metrics and recognizing strengths in the various scenarios.

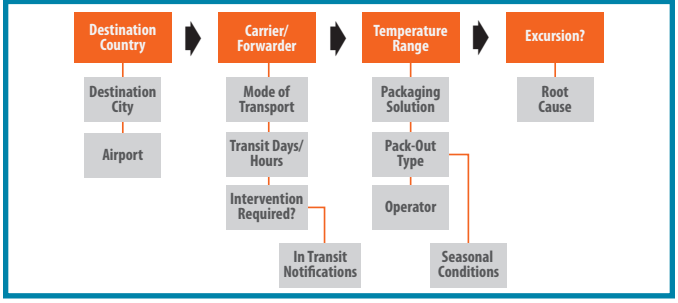
One significant data collection challenge facing the industry today is how to keep track of time out of storage across partners and warehouses. Once a process is developed for tracking this data, it will be an important KPI to review with supply chain partners. Figure 1 illustrates some of the main factors to be considered. Each factor is then subdivided into its critical components to be monitored.

Effectively collecting metrics and KPI's can be very helpful in performing root cause analysis if the correct data are gathered. Even more important is the use of these data in trending to recognize potential areas of weakness before an adverse event is realized. Once noted, these areas can be given additional focus to ensure that the trend is reversed and the supply chain strengthened.

Step 4: Improve internal knowledge in critical areas and of the partners' processes

As the pharmaceutical industry continues to increase its focus on the integration of supply chain partners, it has become more important to understand the processes of partners and increase the firm's internal knowledge to improve coordination between links in the chain. It is

Figure 1. Some of the main factors to be considered. Each factor is then subdivided into its critical components to be monitored.



no longer sufficient to perform flawlessly within a firm's facility; rather, each partner is responsible for ensuring the safe movement of products to final destination.

One way to increase effectiveness between partners is to first analyze the partner's current processes. Once it is understood how partners operate, it becomes more pragmatic to facilitate their success. Of course there are processes internal to the organization that must be adhered to, but if small changes could be made to internal processes to more closely align with the partner's process, the result is a more effective link and limited disruption for the partner. The internal processes and the partner's processes must be evaluated together in order to create the most effective holistic relationships.

Any work that can be performed internally will decrease the time and work required for downstream partners once products reach them. In the international shipping realm, one way to accomplish this is to improve the internal knowledge of import and export regulations. For firms that may not be large enough for a dedicated group of individuals that focus on this aspect of shipping, tools may be implemented to aid in the process. There are many software applications which can help to realize country-specific requirements for documentation and filing [16]. The more accurate the documentation, the less chance of customs delays and possible temperature excursions.

The supply chain must be viewed as a grouping of partners working together with consideration given to each other's link to ensure success.

Step 5: Evaluate and adopt shipping solutions to ensure preparedness for all shipments

As the pharmaceutical industry continues to focus on environmental controls in transit, the shipper's responsibilities also continue to grow. With new shipment temperature ranges becoming more prevalent, the shipper must be prepared to meet the demand with qualified shipping solutions. Coupled with the numerous varying payload sizes, this increases the challenge placed on the shipper and the supply chain as a whole.

New temperature-controlled packaging technologies are continuously emerging on the market [17]. These new technologies not only decrease freight weight and dimensions (cost), but also simplify handling instructions and lengthen qualification periods. Researching these new technologies can lengthen the allowable time to delivery and provide partners with a more solvable problem in the case of delays. Properly vetting these solutions, and when possible, approving them for usage, can significantly aid the firm in reducing temperature excursions.

Another way to broaden the shipping solutions available for usage is to assess those currently being utilized by service-providing partners. In many cases carriers and forwarders offer solutions that can be delivered to the shipper facility to be used for shipment. This will provide a useful resource when a solution is not available at the shipper facility to meet a particular shipment's needs. Another benefit of this type of partnership is that the partner already has extensive knowledge of this solution and has the processes in place to direct its handling. This type of collaboration not only provides a robust solution to meet needs but also allows the partner to work within their area of expertise.

When properly vetted and approved, there are numerous shipping solution offerings that can be used by the shipper facility. Additionally, there are solutions offered by many supply chain partners which can be effectively utilized when the demand cannot be met internally. Having a wide range of solutions available will aid in meeting shipment needs in real-time and ensure a high degree of success at maintaining temperature through the supply chain.

Conclusion

When handling pharmaceutical products in the transportation leg of their lifecycle, there are many challenges which can cause those products to experience a temperature excursion. Therefore, it is imperative to map the supply chain and assure that each and every partner is adequately equipped with the materials, knowledge, and relationships required to ensure safe and effective transport. It is not likely that a firm attempting to focus only on the processes within its own facility will be successful. It requires the collective expertise of all partners to provide the level of service pharmaceutical products demand.

Performing at an optimal level internally is the first piece of the process, but effectively building true partnerships is the key to success. Preparing a shipment for pickup and placing on the dock is only the first step to be monitored. All information and consideration must be given to the downstream partners. Additionally, all shipping solutions and tools must take into account that others along the chain must also interact with them. Implementing these five easy steps will go a long way toward lowering the excursion rate if the appropriate level of attention is given. For BioConvergence, implementing these steps resulted in a 99.7% excursion-free shipping rate the first year of execution.

Note

The principles of this paper were discussed at a workshop presented by BioConvergence, LLC at The 11th Annual Cold Chain GDP and Temperature Management Global Forum on October 2nd, 2013, Chicago, Illinois.

Acknowledgment

The authors would like to thank Robert H. Seevers, Ph.D., Eli Lilly and Company, for his comments in preparing this paper.

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This article was printed in the July/August 2014 issue of *Pharmaceutical Outsourcing*, Volume 15, Issue 4.

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