

Temperature Monitoring in the Pharmaceutical Cold Chain

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Executive Summary

The pharmaceutical supply chain contains vast amounts of temperature sensitive materials. These may be APIs or finished product. During transportation, storage and even manufacturing, temperature excursions outside of critical control limits severely impact product potency and efficacy.

There are a wide variety of products available to pharmaceutical manufacturers for all aspects of temperature monitoring. Some of these products provide digital records, some provide hard copy records, and some can provide both. This white paper presents an overview of available options and what can be expected from each for regulatory and record keeping purposes.

Introduction

Globally, regulatory agencies continue to increase their oversight for ensuring the integrity of pharmaceutical products. This governs practices and procedures for both distribution and storage. With many of these new regulations, temperature monitoring is a key element.

Temperature monitoring needs to be approached with a full picture perspective. To think that nothing can or will go wrong during shipping and/or storage is naïve. Many things can and do happen, especially when there are multiple handoffs between manufacturing and the end user. And ultimately, responsibility for the safety and effectiveness of finished product lies with the manufacturer. A record that shows temperature history is like an insurance policy for your product. It serves to validate that no excursions have hurt your product, and it can also point to accountability if an excursion does occur.

At the 6th Annual Cold Chain Distribution for Pharmaceuticals Conference in Philadelphia (Sept 2008), numerous speakers stated that human error was the cause of many temperature related problems. Whether these problems were from lack of training, disregard of standard procedures, unexpected delays during transport, or some other factor, the bottom line is that product safety and efficacy was compromised.

Temperature monitoring itself does not guarantee that product quality is maintained. It can however show if there was a problem and who had possession (responsibility) at that time.

Temperature Monitoring Options

There are numerous tools available for monitoring temperature. These include:

- Data loggers
- Facility (wireless) systems
- Chart recorders
- Thermometers
- Thermal labels

While this appears to be a simple enough list, it must be stated that there are numerous crossovers between these tools. It should also be recognized that quite often, a combination of tools could be required. Consider areas where electricity may not be available. A data logger might be good for transportation all the way to an airport, but from there, without electricity, there would be no way to extract temperature information beyond that point. Beyond the airport, a strip recorder or thermal label could be a better choice for providing critical temperature information.

Solutions for Transportation

Temperature monitoring during transportation is a critical component in the cold chain. It must begin with the manufacturer and hopefully it will end with the consumer. In some situations this is much easier to do than in others. Vaccines that are distributed in hospitals are much easier to monitor than are vaccines distributed to remote areas of developing countries.

One consideration for temperature monitoring during transportation is thermal mapping of the shipping container. Large containers such as those used with truck transport or sea transport may show temperature variations at different locations. An obvious example would be temperature measurements at the top and bottom of a container when air was not being circulated. Another example relates to extreme hot or cold conditions, where product in close proximity to outer walls might have a different temperature than product in the center of the container. For this reason, it is often beneficial to use multiple devices in a container and record which unit is in which location.

Traditionally, strip chart recorders (analog devices) have been used for monitoring temperatures during transport. These devices are inexpensive and provide a temperature history on a strip of paper that is extracted by the receiver. The receiver can then view a temperature history and determine if that product is safe. These devices are available with various time periods, typically ranging from 5 days to 90 days. The one factor to consider for these is resolution. It is best to use devices that support a time period slightly longer than the scheduled trip.

For many companies, data loggers (digital devices) have replaced strip chart recorders. These are electronic instruments that store temperature information in computer memory. This temperature information is then downloaded by the receiver. These loggers are available as single use or multi-use devices, and like strip chart recorders, are available with different logging periods. One distinction between analog and digital instruments is that the analog units write a continuous line on the recording surface, where digital units take and record a measurement based on their sampling period.

Another tool that can be useful for transport monitoring is thermal labels. These devices provide pass/fail information and are often available where they can also incorporate a time element. They are low cost, single use indicators that undergo a visible and irreversible change when temperatures go beyond a set threshold. They are available with either ascending or descending temperature thresholds.

Depending on the circumstances for any particular shipment, single or multiple solutions could be best. With vaccines targeted for remote locations, it could be best to use a combination of monitoring solutions where thermal labels are on individual vials and data loggers are used during air, sea or ground transportation. It might even make sense to use data loggers for the beginning of the journey and then strip chart recorders to the final destination.

Another option for monitoring temperature during transport, although not as common as the others, would be min/max thermometers. These instruments are inexpensive and will store minimum and maximum temperatures until reset. These are a great solution for places where product might be stored temporarily and the holding organization does not have access to loggers or recorders that are positioned inside a payload. With these, the holding organization can monitor their handling without impacting the manufacturer's temperature monitoring system. These are also a great tool for container cool down as part of preparation for product loading.

One final temperature monitoring system that needs mentioning here involves radio frequency identification (RFID). These systems are starting to become available, but as of this writing, could still be considered to be in their infancy. They do however offer some very interesting capabilities.

RFID systems may be passive, active, or a combination of the two (semi-active). Passive systems do not collect any information, but can be used as locators inside a payload. Semi-active systems collect data that can be retrieved later. Active systems are data loggers that can record and transmit data. With regard to RFID data, this is not limited to temperature (or humidity) information, but could also be used as GPS transmitters when tracking payloads.

With each of these temperature monitoring solutions, there is an element of record keeping. Data loggers can provide hard copy and/or computer based records. They also offer the capability for statistical analysis. Recorders and thermal labels are limited to hard copy records. In the case of vaccines and other medicines, thermal labels may simply act as an indicator of whether or not that dosage is fit for administering.

Data loggers store digital data that can be printed on a portable printer, downloaded to a desktop application, or uploaded to a web-based data management system. In the case of the desktop and web based scenarios, users can view data tables or graphical analysis of applicable temperature history. They can also access a variety of statistical information from the temperature history. All of these systems enable users to create archives for full traceability.

One other option available with data loggers is the ability to write a PDF file directly from the logger without any operator intervention. These files are portable and can be emailed or easily shared. They can also subsequently be archived for record keeping purposes.

With regard to regulatory compliance, both hard copy and computer based record keeping have their pros and cons. In the United States, the Food and Drug Administration (FDA) has put forth a directive for current Good Manufacturing Practices (cGMP) titled “21 CFR Part 11”. This addresses electronic record keeping requirements. The purpose of Part 11 is to set procedural and instrument controls for the integrity and confidentiality of electronic records and signatures. There is a wealth of information available on the internet pertaining to 21 CFR Part 11.

Solutions for Facilities

Pharmaceutical facilities may contain a wide variety of rooms and equipment for storage and manufacturing of temperature sensitive goods. As is the case with transportation systems and temperature monitoring, different solutions are available, depending on circumstances.

One of the first considerations for a facility installed system is the level of operator intervention. Traditionally, facilities have installed either thermometers or chart recorders. With thermometers, an employee was required to periodically view and record temperature data on a form. With chart recorders, an employee was required to change charts in the recorder based on the time period of the chart. In both scenarios, hard copy archiving was implemented. With these systems, operator error (forgetting to take action or recording inaccurate information) was not as infrequent as would be expected. Advances in technology brought automated systems that no longer rely on human intervention for maintaining temperature history records.

Automated systems can be in the form of data loggers or wireless systems (transmitters and receivers). Both these scenarios provide temperature (and/or humidity) data that is uploaded into a computer system for archiving and statistics. Like the mobile systems, data management solutions can be either a desktop application or a web hosted service. Data logger systems require operator intervention in the form of getting data into the computer system. Wireless systems require no operator intervention. They will record data and get that information into the computer with full automation.

Wireless systems rely on a few different components. Sensors measure environmental information, transmitters send that information to a central location, and receivers collect the data from the transmitter and add it to the environmental history database. In many cases, repeaters are also needed to extend the range of the transmitters. Repeaters assist with getting the environmental data to the central location over long distances or through physical barriers such as walls in temperature controlled rooms.

With facility installed systems, alarm systems can be set up to notify appropriate people in the event of any temperature excursion. This is an excellent solution for off-hour periods and protecting high dollar commodities. Consider the consequences of a refrigerator or freezer compressor failing during a long weekend. An alarm system could save untold dollars worth of APIs or products from damage due to temperature abuse.

Alarm systems offer numerous options for notifications. In the event of a temperature excursion in any monitored area, the system can initiate text message, voice, or e-mail notifications. On top of this, the system can also direct that notification to specific individuals based on time of day or week. One other option that can be added to the notification system is electronic messaging boards. These provide visual status for the monitoring system. These are fully programmable and offer users the ability to show not only that a temperature excursion has occurred, but where that incident happened.

Thermal labels could also be considered for monitoring temperature in manufacturing facilities and warehouses. While these are not typically designed for this type of use, they do provide fail safe backup for whatever system is implemented. These labels may be temperature sensitive or time-temperature indicators where they can show a time element for temperature excursions.

Summary

Temperature monitoring is an important part of the pharmaceutical supply chain. Regardless of whether you are a manufacturer, transporter, or distributor, the fact remains that temperature sensitive products and materials must be handled appropriately. A major part of this handling involves cold chain management. And good cold chain management should result in a full, traceable temperature history.

There are a wide variety of tools, both analog and digital which are available for cold chain management. These may be used individually or in combinations. Their common goal is to help ensure that final product quality and efficacy is maintained. They also can help you meet regulatory compliance by providing a full temperature history, complete with traceability.

About DeltaTRAK

DeltaTRAK, Inc., is a leading innovator of cold chain management and temperature monitoring solutions. Their product line includes a wide range of temperature and humidity data loggers and wireless systems. They also develop and manufacture high quality portable test instruments that monitor / record temperature and humidity. One additional component of their full line of cold chain management systems is professional digital probe and infrared thermometers.

In support of DeltaTRAKs cold chain management solutions, they offer management / analysis software for the data logger and wireless system product lines. Their products and services are depended on by businesses big and small around world.

ColdTRAK®, a web-based software solution from DeltaTRAK, provides validation and quality assurance functionality as related to cold chain management. Industries served include pharmaceuticals, chemicals, adhesives, and food / food safety. Any business with temperature-sensitive commodities, inclusive of processing, manufacturing, storage, shipping, and handling, can benefit from implementing the ColdTRAK system.

DeltaTRAK also offers third party certified calibration services. This can be used to support compliance, traceability, validation, and quality assurance programs. Calibration services may even be used as evidence for insurance claims pertaining to improperly handled temperature sensitive commodities.



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