PRACTICAL GUIDE

7 Reasons Why Cold Chain Monitoring Is a Big Deal

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Cold Chain Monitoring – Seven Important Aspects From the Stakeholders' Point of View

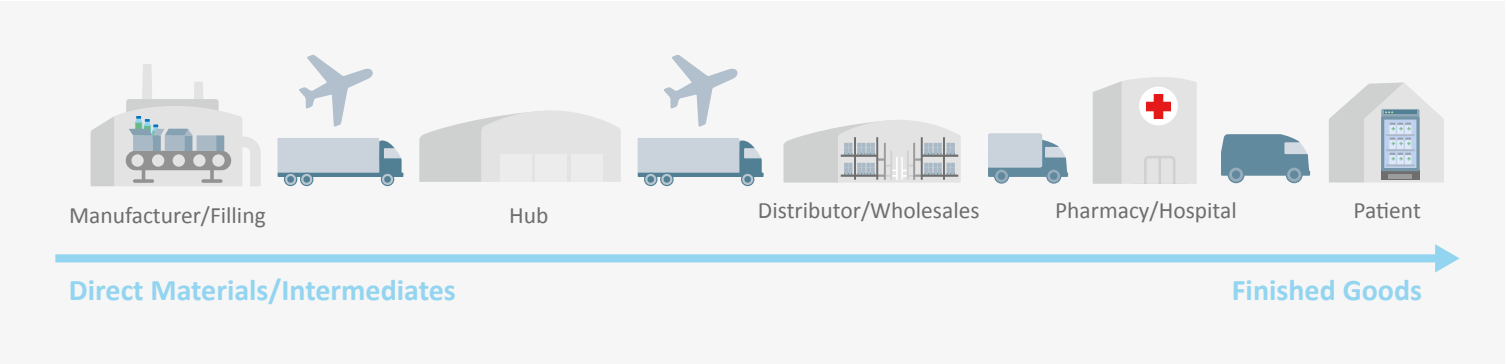
Starting from active pharmaceutical ingredients (API) and ending in the hands of the patient, the quality of pharmaceutical, health care and life science products is preserved by maintaining environmental conditions predetermined by the manufacturer. Monitoring of these conditions in along the journey is a regulatory requirement and must be traceable and in full compliance throughout the entire cold chain. Cold chain monitoring systems are designed to notify you of potential risks an excursions in the predetermined environmental parameters to ensure and document safe and successful delivery.

Manufacturers, logistics personnel, warehouse managers, medical providers, quality assurance managers, will all agree that proper environmental monitoring is absolutely essential to maintaining GDP and GMP-compliant cold supply chain success. Below is a list of seven important aspects of cold supply chain monitoring, as determined by key stakeholders.

Reason 1:
Improved Product and Patient Safety

Cold chain monitoring plays a vital role in providing proof for efficacy and ensuring patient safety. This is always the highest "overarching" priority: to eliminate or mitigate risk to end-user patients by closely following manufacturer's specifications and the regulatory guidelines set forth by various authorities.

Before manufacturing and distribution, the product undergoes rigorous testing to detemine safe shipment and storage conditions. Many parameters are taken into account,



Simplified version of a pharma supply chain

such as sensitivity to humidity, temperature, shock, light, and many others. Testing also determines the amount of time the product can spend outside of its specified range of "ideal" conditions without compromising its quality, or efficacy. Sensitivity to humidity, temperature, shock, light and many other parameters are also considered to determine a suitable "stability budget" for products. By determining the product stability budget, managers can ultimately implement strategies to best prevent drug shortages and ensure critical drugs reach patients safely and in time. This calculated stability budget is programmed into an environmental monitoring solution and configured to alert a responsible party when conditions begin to deviate.

Having access to reliable, secure and compliant environmental monitoring data captured throughout the entire cold supply chain, responsible parties can easily determine if products are safe for consumers or if they have been compromised.

Reason 2: Guaranteed 100% Compliance

Pharmaceutical regulating bodies have defined temperature monitoring requirements for the storage, production and distribution of medicines, vaccines, therapies, and medical devices within Good Practice (GxP) Guidelines. The ultimate goal of these GxP guidelines is consumer safety.

Below are a few examples of these requirements:

- Produce, handle, store, and transport products in qualified facilities, cold rooms, containers, insulated boxes, reefer trucks, vans, utilizing validated data loggers and software for evaluation and archiving of measured data.
- Qualification always starts with the definition of the intended purpose and then continues with an evaluation and documentation of whether the equipment is suitable to fulfill the intended purpose. This evaluation often includes a temperature and humidity mapping of the said equipment.
- Ensure the temperatures are monitored by a compliant monitoring system (which would include an audit trail) that records product deviations from specifications.

Data integrity is the assurance that your data are recorded accurately, maintained in a secure, validated environment (free of manipulation) and compliant.

To be compliant there must be an audit trail showing that you indeed carried out your requirements. Temperature monitoring systems are designed to collect all the required information, proving data integrity, data organization and user access. An audit trail usually documents all manipulation within the system. It typically includes details such as:

- Changes of acceptance criteria or of the configuration as such
- Configuration of shipments and data logger(s)
- Temperature deviations, status, and changes to settings
- Warnings and alarms: Who has the system informed and when?

- Comments, reassessments, and releases: who has commented on shipments, performed manual or automated reassessments, and finally released products?
- Generation of reports, i.e., which user did create which report
- Changes in the user management (new users, deactivated users, changes in user roles and rights)

Failure to comply with regulations could mean authorities will require a detailed plan to address each violation. In escalation, authorities can issue a warning letter; submit import alerts on your products; pursue a court issued injunction, criminal prosecution, and ban you from the industry.

Outside of legal consequences, a series of hardships can also cascade from violations:

- Death or harm to patients, or the potential to do so
- Dissatisfied customers and critics
- Loss of credibility, bad reputation
- Product returns
- Increase of product waste
- Lost business

Reason 3:
Proving Efficacy and Reliability

There are numerous errors during a product's cold chain journey that can cause prolonged excursions outside of the allowable temperature ranges or other monitoring parameters. The unintended exposure can shorten a product's shelf life and cause it to deteriorate. In some cases, the product may transform into a completely different substance! Decreased potency may mean minimal protection against a disease. Once potency is lost, it cannot be restored. If an ineffective vaccine is administered, patients will likely need to be revaccinated. If the treatment lacking efficacy is a patient's only option, it is quite possible they succumb to an illness that was otherwise preventable or curable.

In these cases, right temperature monitoring system could alert responsible parties, which could, in turn, save the products, save the patients, and save your business.

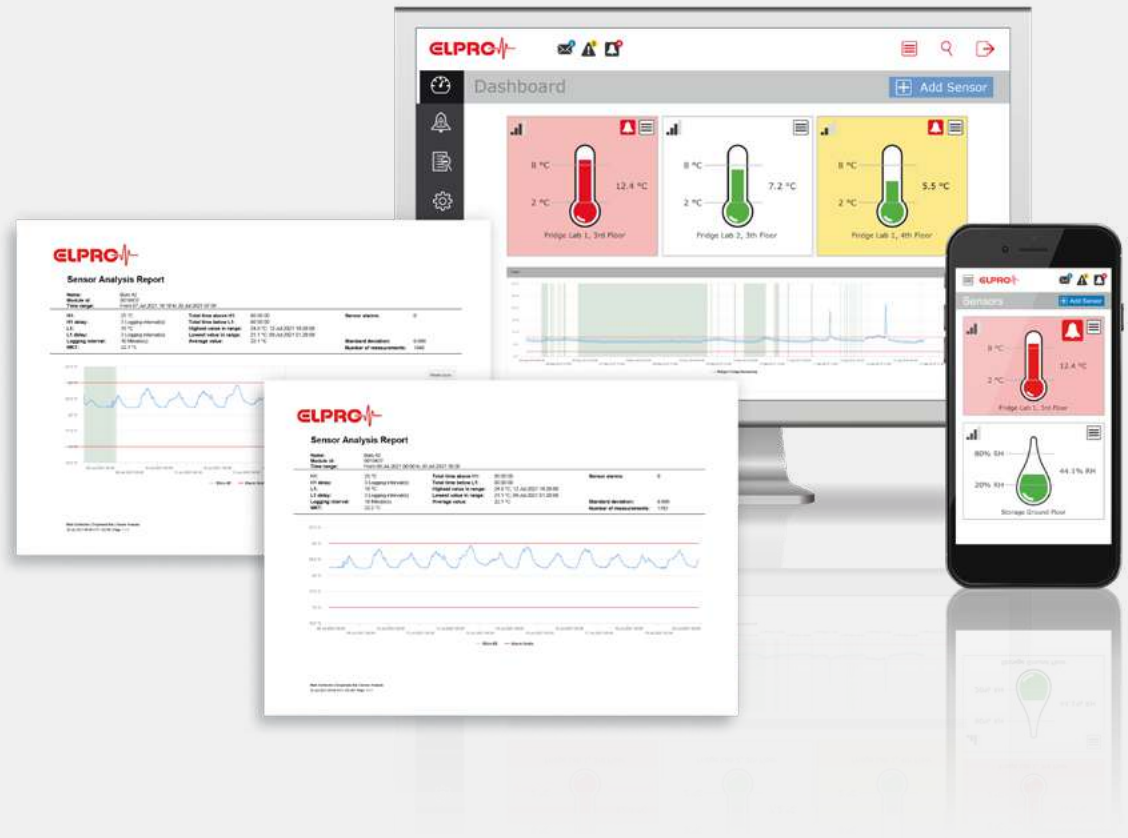
"Monitoring technologies are key to managing processes, including logistics and shipment tracking and documentation."

Reason 4:
Packaging and Distribution Challenges

Even if products are prepared for distribution with the strictest risk assessment, and even if your logistics plan has backup plan, safeguarding product quality is still a constant battle with unfortunate events. Below are a few examples. The only way to usurp threats to product spoilage is to be proactive and react immediately to temperature excursions.

Pickup/Drop-Off Delays

When consignments await the next leg of their transportation, containers could be exposed to uncontrollable ambient conditions. Schedules are often compromised because of import complications, supply chain staff, resource shortages, and so on. Unanticipated events like accidents, extreme weather, outages, natural disasters, crime, pandemics, war and/or political interference may be a cause for transportation reroutes and delays.



Loading and Storage Failures
Passive containers typically require particular loading requirements that include a variety of elements, such as vacuum insulated panels, dry ice and phase change material (PCM). If a box or tank is not secure, the cooling or insulation properties could be jeopardized. Products could be positioned too close to turbines or doors.

Technical Failures and Human Error
Here are some examples of where human error, lack of infrastructure and/or planning can be detrimental to a shipment.

- Specified equipment may not be fit for use.
- Active containers/trucks contain hundreds of different mechanical parts that can fail.
- Temperature data loggers are not stopped or started at appropriate times, resulting in data gaps or data loss.
- Airflow around active containers could be blocked.
- Recharging or charging or cryogenic tanks or dry ice packing/repacking doesn't occur as planned.

Adequate procedures and precautions must be enforced to prevent damage, degradation, quality issues or a total loss of a shipment.

Reason 5:
Enhanced and Simplified Organization

When it comes to daily activities such as analysis, product release, reporting, archiving, not to mention audits, quick and easy access to your data is imperative. The right environmental monitoring system can organize and automate these activities and required manual tasks. By design, cold chain databases are engineered to meet regulatory compliance and mitigate the risks of:

- Forgetting to equip shipment pallets with sensors
- Starting or stopping sensors incorrectly
- Failing to upload the data files from USB data loggers
- Losing real-time connections to loggers

Automated features can include:

- Operation performance status (to trigger a system warning)
- Sensor status, to include currently measured values, the alarm status, time stamps, statistics, setting changes, warnings – any technical status of the sensor
- Sensors can be grouped in a meaningful way (i.e., per shipment, per product, etc.)
- Data logger information (battery status, wireless connection, validity of the delivered data to trigger sensor warning)
- Measuring, storing, and evaluating temperature values and matching them with the defined limits to trigger high/low temperature warnings and alarms
- Generation of regular reports including sensor names and groups, timeline, user which has created the report
- Assigning of profiles with allowable temperature ranges
- Uploading of shipment preparation data and data files of all measurement
- Evaluation of measurement data to determine a positive or negative release decision
- Notification to stakeholders identifying the status of a shipment or monitored product

Cause of False Excursion	Cold Chain Database Intervention
Early start, sensor measures too early (before product has been loaded or conditioned)	Cold chain database can reassess the data using the correct time stamps
No temperature values available due to sensor failure (sensor not started or no sensor added)	If the shipment contains more than one device, it might be possible to use the data from the other sensors to release the entire shipment
Minor temperature excursion during shipment	Cold chain database can reassess the data using the stability data of the product
Wrong sensor setting triggers a temperature alarm	Cold chain database can reassess the data using the correct stability data
Late stop at destination, sensor continues to measure (at room temperature)	Cold chain database can reassess the data using the correct time stamps

Common causes of "false alarms" and possible cold-chain database interventions

Reason 6: Improved and Faster Processes

For sustainable corrective and preventive action (CAPA) for cold chain management in your organization, a database is necessary to provide visibility to issues in a structured and well-documented way. A central repository of temperature data allows for examination of recurring excursions on specific routes, depots, or at logistics partners over longer periods of time.

Sometimes additional criteria are defined, such as the number of allowed excursions or the number of freeze-thaw cycles. Visibility to this data enables assessments to be performed and a clear OK (= release) or ALARM (= quarantine) decision can be made.

With the right temperature monitoring system, it is easy to analyze the data to find and prevent problems in a proactive way. Leading solutions are also able to intervene during false excursions.

One Example For Improved Process: Clinical Trials

Onsite monitoring or traditional monitoring processes can be a time burden for both sponsors and site monitors during clinical trials. Remote monitoring – on site sensors are manageable and accessible remotely via web access – has minimized the travel and communication delays, thus increasing the overall speed of the trial. Real-time monitoring platforms allow monitors and sponsors to access data within seconds and as frequently as needed. Even outside regular working hours, thus, increasing efficiency and effectiveness. By using less time, the monitor can focus their attention on other aspects of the clinical trials, and this will result in better quality trials.

It eliminates the need for paperwork. Traditional monitoring uses paper-based methods, which limit the ability for repeatable processes making them less efficient. It is burdensome to physically store and organize large quantities of research documentation. Real-time monitoring can be built into a process all at once, and data can be duplicated, and monitoring can be executed only by a few clicks. The user can create customized document templates, which can be duplicated across other sites and studies, and they can be stored without the need for physical space.

Reason 7:
Avoid Product Waste

There are several ways to prevent product waste by using a temperature monitoring system. Two of the most important are real-time monitoring and the implementation of an excursion allowance model.

Real-time monitoring systems are proactive intervention technologies that continuously keep track of the state of the environment of the product. They provide immediate information any time. The technology systems used in remote monitoring include features that allow streamlined communication, customized data dashboards, email/SMS alerts, and in-app messaging and reporting. Information is readily accessible with very little latency at any time and from any location as long as the device is connected to a mobile network. By doing so users can identify shipments that are likely to experience delays and intervene accordingly at any stage of the supply chain journey.

Another way to avoid waste is by implementing an excursion allowance model. Such a model uses information from stability testing where a stability "budget" can be programmed into a temperature monitoring system allowing users to determine whether or not a product is still of good quality after it has experienced a temperature excursion. A stability budget prevents expensive, time-consuming investigations with contract research organizations (CRO) and logistics service providers (LSP). Using this model means delays can be avoided, fewer products will be discarded, shipment are released faster and costs are reduced.

Conclusion

Environmental monitoring solutions are critical to safeguarding product integrity and patient safety, guaranteeing full compliance in your cold chain supply. They also work hand-in-hand with active and passive packaging solutions to enable improved processes and automation, provide access to critical data (resulting in faster release times), and promote sustainability by eliminating product waste.

Temperature Alarm Zones

	Used	T [°C]	Alarm after		Event	Excursions
H4:	☐	0	0	Minutes	Single	unlim.
H3:	☑	30	0	Minutes	Single	unlim.
H2:	☑	25	2	Hours	Cumulative	unlim.
H1:		8	12	Hours	Cumulative	unlim.
G:		2	No Alarm			
L1:		0	1	Days	Cumulative	unlim.
L2:	☑	0	0	Minutes	Single	unlim.
L3:	☐		0	Minutes	Single	unlim.

☐ Zone H1 and L1 coupled

Based on the stability data of a product – in this case a +2 °C to +8 °C product – data loggers can be configured to allow a specific time outside of range without a deviation occurring (stability budget).

This practical guide is part of the Cold Chain Monitoring Solutions & Logistics website content for supply chain and QA professionals. Topics include information on product integrity, patient safety, compliance in your cold chain supply, active and passive packaging solutions, processes and automation, and sustainability.

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