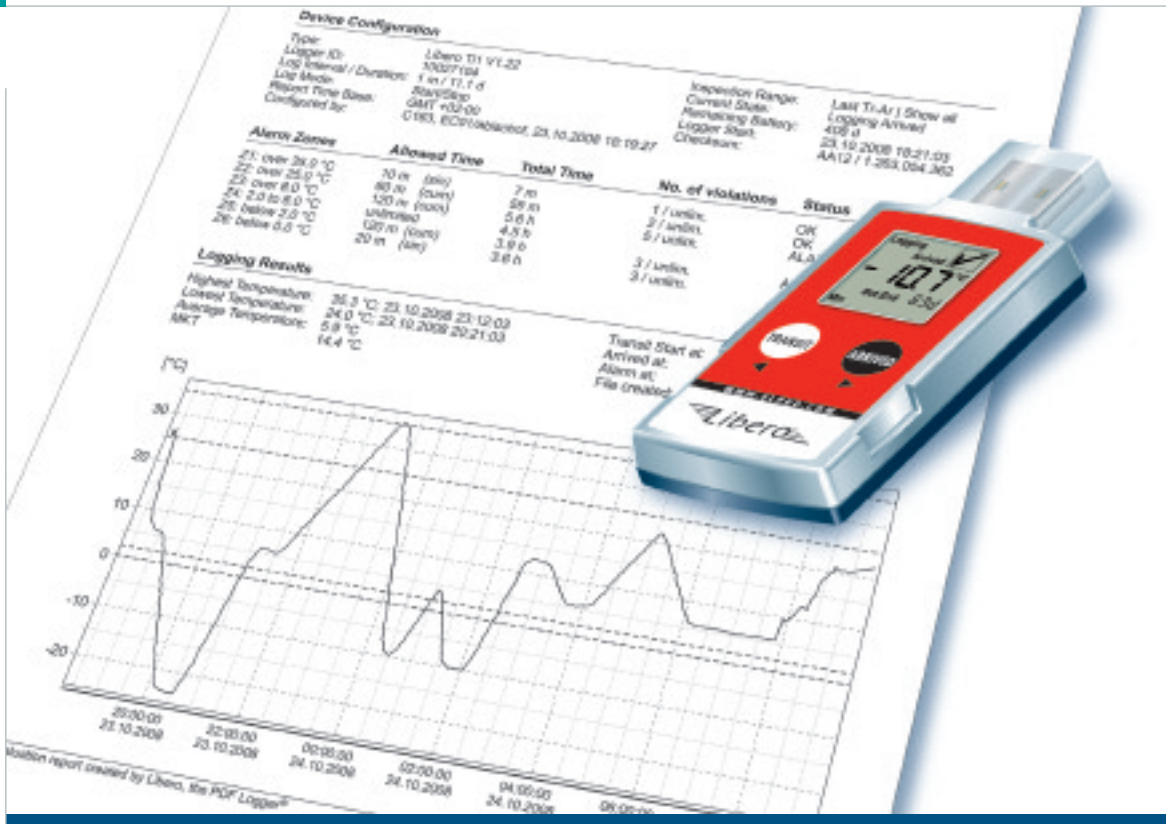


Avoiding Data Overload

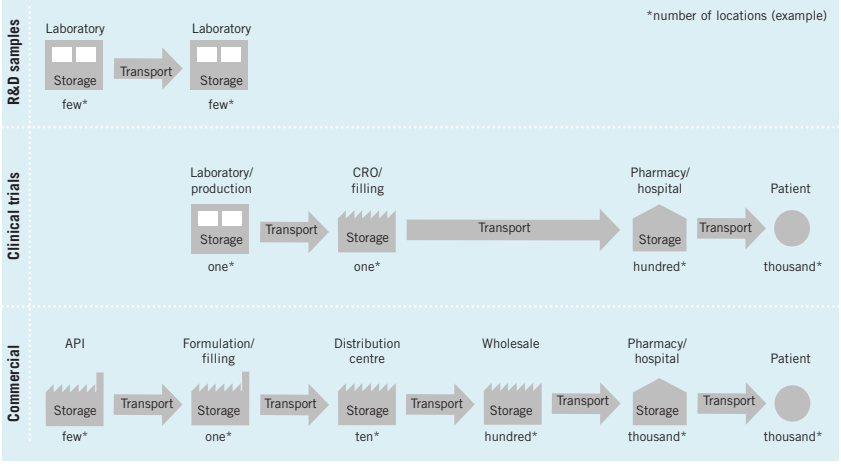
Thousands of temperature-sensitive pharmaceutical products are being shipped daily accompanied by data loggers to track their temperature during transportation. What are the best approaches to dealing with the challenges of data management in the pharmaceutical cold chain, asks Martin Peter at ELPRO-BUCHS AG Switzerland

The term 'cold chain' generally refers to the transportation and/or storage of temperature-sensitive materials, from active pharmaceutical ingredient (API) to final product. By definition, monitoring of temperature and other physical measures, such as humidity, is therefore always an integral part.

Although an increasing number of experts and industry guidelines define the owner's responsibility with regard to product integrity over the entire end-to-end supply chain, many companies only focus on certain parts of the chain – for example, up to the point where responsibility is handed-over to the wholesaler. Additionally, the various phases in the development cycle of a product (R&D, clinical trials and commercial) are considered separately. Nevertheless, even though the focus is on just a few steps in one phase within the chain, it remains a complex issue, and data management is a considerable challenge.

It is important to consider difficulties such as: how to collect the data from several countries; where to store the data and how to give access to the right people; and how to allocate

Figure 1: Generic cold chain in the pharmaceutical industry



Source: Martin Peter, ELPRO

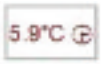
additional information to the cold chain data.

DATA MANAGEMENT

Data management encompasses the collection, availability and use of (temperature) data, and the integrity of products during transportation and storage. When using the terms 'data' or 'cold chain data', it is vital to define the various elements.

When using this terminology, two kinds of data management can be performed: finding reports (based on additional information); and analysis of a single or multiple 'curves'. A typical search example would be to find all winter shipments from Zurich to Moscow which had an excursion of less than 0°C; whereas a typical analysis example would be overlay all LMV (graphs) from the example search, calculate an average and add marker points accordingly.

Table 1: Definition of cold chain data

Data term	Symbol	Definition	Example
Measured value (MV)		One measurement value (or reading) of a temperature monitoring device at a defined time and place	5.9°C, 12:47, 4 Jan 2011
List of measured values (LMV)		A list/sequence of (temperature) measurement values usually representing a segment in the cold chain (storage or transport) – typically looked at as graph	List of MV during transit or storage
Assessment criteria (AC)		Limits (temperature levels and times) representing the success criteria of a shipment – usually linked to the stability data of a pharmaceutical product	OK if between 2 to 8°C and not more than 24 hours outside 0 to 15°C
Report (R)		A report combining LMV and AC to draw conclusions (OK or ALARM) on a shipment or storage – typically used as the basis for a product release	LIBERO PDF report
Additional Information (AI)		Additional information describing the LMV (for example, shipment information)	Product: Vaccine 1 Origin: Zurich Destination: Moscow Logger placement: inside box Box type: insulated box xyz Forwarder: xyz Mode of transport: air

Source: Martin Peter, ELPRO

WHY IS IT IMPORTANT TO COLLECT DATA?

In the past 15 years, millions of shipments have been performed and the products were released without the need of data management. So why should it suddenly become important to collect temperature information and manage data? There are three key reasons:

Are You in Control?

Data management is designed to safeguard the integrity of the product. Cold chain data systematically collected and managed helps to measure the effectiveness of the chosen packaging materials, processes and service providers, for example:

- Is your packaging qualification as effective in the real world as they have been when tested?
- Are there any changes to your distribution environment?
- What is accountability of service providers?
- Are there any opportunities for cost savings?

Legislation

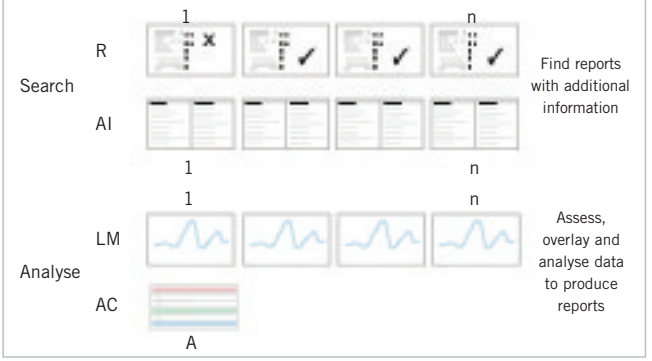
An increasing number of guidance documents define data management as a regulatory requirement – for example the PDA Technical Report 39, which stipulates that the shipper must collect and archive GMP relevant data for 10 to 20 years in a safe place and in a suitable format (1).

Efficiency

Data management can speed-up the release process. When collecting cold chain data and making them available to organisational units, the release process can be shortened by improving their availability, so that reports are available in electronic format ready to be archived (PDA/A for archiving), as well as making use of automation, whereby ALARM reports are automatically forwarded to quality assurance (QA).

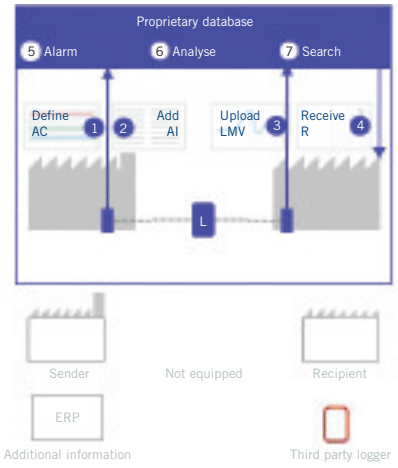
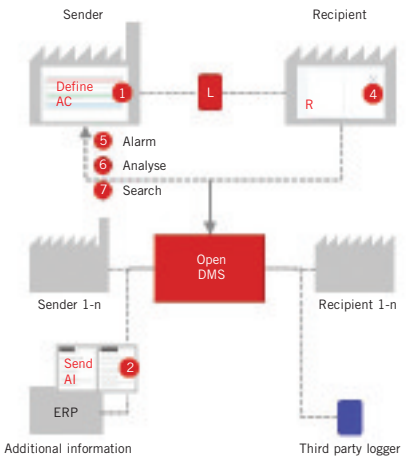
As a result, pharmaceutical companies are increasingly expressing the wish to systematically collect and use cold chain data. Successful projects are motivated by improvement of quality, which safeguards integrity, and/or process improvements, which speeds up the release process. Before starting a data management project, one should define why exactly you want to collect cold chain data (for example, to monitor effectiveness of a chosen packaging method), and what kind of analysis you want to perform (for example, to find reports per trade-lane and count the number of excursions).

Figure 2: Data management models



Source: extract LIBERO Monitoring of ELPRO

Table 2: Two fundamental approaches to data management in the cold chain

	Proprietary database	Open document management system (DMS)
Summary	Proprietary databases are typically web-based databases provided by the monitoring solution producer as a service with a dedicated connection, interface and cable at sender (for shipment start) and at destination (for shipment end and upload). The system is neither open to non-equipped sender/destinations, external data sources nor to third party dataloggers	Open document management systems are typically based on standard document management systems and have the capability to work in an open environment without the need of equipment or dedicated connections. The system is open to any sender/destination, to external data sources and to third party dataloggers
Illustration		
Start a shipment	Sender activates a preconfigured logger. Using a dedicated connection and interface the shipment can be started and the logger allocated	Sender customises and starts the logger with an identifier (for example the shipment number). A configuration report is automatically mailed to the DMS
Add information	Additional information can be added manually to each shipment by logging on to the proprietary database using drop-down lists	Additional information (usually electronically available in sender's ERP system) is automatically mailed and mapped (using identifier)
End a shipment	Recipient stops the logger and uploads the data via dedicated connection and interface. Online, an assessment is performed and a report can be generated	Recipient stops the logger, automatically performs a PDF report and releases the product. The report with raw data is mailed and automatically processed by the system
Advantages	• Full control over shipments • Destinations are forced to upload data • All in one: finding the data and view/overlay	• No equipment needed – use email or upload • Open to any sender and recipient • Open to additional information • Open to third party loggers
Disadvantages	• Equipment needed at sender and recipient • Additional info must be added manually • No third party information	• Destination is not forced to upload • No full control over shipments • Separate tool needed for overlay many graphs

Source: Martin Peter, ELPRO

Thus to summarise, before starting with cold chain data management, it is important to agree on a rationale for the project, and define your expectations for the analysis it will produce.

DATA CHALLENGES

A range of challenges await any company trying to collect and manage cold chain data systematically.

Data Collection

When collecting data from shipments to and from worldwide destinations and storage facilities, a number of factors should be considered. Consistency is key: one must make sure that all the data available is collected. Speed of access to the data is also important. System and equipment requirements should be kept in mind, especially if extra equipment is needed at the destination in order to return data. Finally, ease of use is another important factor: is there a need to return, monitor and manually upload or is it possible to perform an on-site assessment?

Release Process

Before the release of a product, a decision must be taken based on the collected data, taking other variables into account. For example, is the right information available, and what are the assessment criteria at the destination? Data security is important too; the data should not have been manipulated. Likewise, one should

Cold Chain Monitoring: The Traditional Way

Traditionally, the cold chain monitoring process used pre-configured data loggers that were started at origin and placed with the temperature-sensitive products. At the destination point they were unpacked and analysed by means of specific equipment (for instance an interface or cable) and software. This software allowed for the production of a report, including alarm statistics and graphics summarising the compliance of the measured temperature during the journey versus the acceptance criteria. If at destination no equipment and software was available, it was necessary to return the datalogger to the sender for analysis. The sender was then able to make a judgment on the condition of the goods and provide the product release. The challenges with this process included: missing equipment at the destination; a lack of standardisation; time lost at product release; and a lack of an available data archive.

look in to whether there are any tools that can automate the process.

Security

The integrity of the data is vital. Can it be guaranteed that it is impossible to manipulate the data? Is the access to the data limited to the right people/organisational units? And, is a document control process installed to avoid duplicates and redundancies?

Finding Data

Once temperature records are collected in a database, the challenge becomes how to find them. A search can only be conducted within pre-assigned fields, and furthermore, the search only delivers results if the pre-assigned fields are filled with information.

Feed the System with Additional Information

Reading information available on a datalogger is simple – but how does the additional information get into the system? Does the analyst need to enter information from another system? Centralised control is important; with manual entry there is no control over consistency and opportunity for errors creeps in. Automating information hand-over can help, but system integration can be expensive and difficult to implement.

Another important point to consider is that a database can only be fed automatically if a 'key' is available to the raw data of the logger files. In our eyes it is not acceptable that a separate database must be maintained for each manufacturer/logger type. But unfortunately, most logger providers do not have an 'open source policy' and only offer proprietary systems.

Therefore, it is important to work with a provider that offers a validated solution. This means that additional information can be fed from another system (such as ERP), with an open source policy that allows the use of one database for various dataloggers.

COST OF DATA MANAGEMENT

When looking at the cost of data management in the cold chain, it is essential to take a total cost of ownership (TCO) perspective of the entire monitoring solution. It is impossible to separate the cost of monitoring from the cost of data management. Additionally a TCO-view only makes sense when comparing two different options (for example, TCO monitoring today versus the implementation of a new system). In the following analysis we focus on an example TCO analysis for cold chain data management of a proprietary database versus open DMS.

The cost and benefit is driven by requirements (for example, what functionalities and processes need to be covered to achieve your goals?) and the degree of automation (for instance, which processes should be automated and which should be carried out manually?). For simplicity, we look at cost per year and consider all investment and equipment that will depreciate over a 12-month period. This is in fact a realistic assumption considering the speed requirement

Table 3: Example of total cost of ownership comparison for 1,000 shipments per year

			Proprietary database			Open document management system		
	Cost type	Number per year	Unit cost ($)	Cost per year ($)	Comments	Unit cost ($)	Cost per year ($)	Comments
Equipment sender	Direct	1	100	100	Each sender needs to be equipped with interface, cable and connection to database	-	-	No equipment needed at sender
Training sender	Process	1	200	200	Keep personnel at sender up to date (including interface, activation, opening of shipment and adding information)	200	200	Keep personnel at sender up to date (including configuration and adding shipment number)
Direct logger cost	Direct	1,000	30	30,000	Cost to purchase dataloggers (single use)	60	60,000	Cost to purchase PDF dataloggers (single use)
Activate at sender	Process	1,000	-	-	Monitors are preconfigured	1	1,000	Configure datalogger and add identifier (shipment number)
Add information	Process	1,000	10	10,000	Open shipment in database, connect logger to database, edit/ enter additional information	-	-	Additional information is automatically added
Equipment recipient	Direct	100	100	10,000	Keep personnel at recipient up to date (including interface, activation, opening of shipment and adding information)	-	-	No equipment needed at recipient
Training recipient	Process	100	200	20,000	Effort to keep personnel at recipient up to date (including interface, upload and view report)	-	-	No equipment needed at recipient
Stop at recipient	Process	1,000	-	-	Stop logger at recipient	-	-	Stop logger at recipient
Upload/report	Process	1,000	10	10,000	Use interface to perform upload to database, automated assessment, report is generated	3	3,000	PDF report is automatically generated (including raw data). Send via email to DMS
Release	Process	1,000	-	-	Process of release (in case of alarm, further investigation by QA)	-	-	Process of release (in case of alarm, further investigation by QA)
System cost	Direct	1	20,000	20,000	Fee for hosting, availability and maintenance of the database	10,000	10,000	Fee for hosting, availability and maintenance open document management system
Transaction-based fee	Direct	1,000	20	20,000	Transaction-oriented fee usually charged per shipment or alarm	-	-	No transaction-oriented fee
Total cost		**1,000**	**120**	**120,300**		**74**	**74,200**	

Source: Martin Peter, ELPRO

changes as well as the industry's regulatory habit of limiting equipment calibration/validation to one year. But even more sensitive are the assumptions surrounding the process cost, which could also be described as the time and effort needed to perform a single process step. By definition, a cost comparison is only an approximation of reality and is driven by the assumptions – but it is helpful to understand the cost drivers and their dependencies (see Table 3).

It is clear, therefore, that organisations should only chose a proprietary solution in a clearly defined and limited set-up. Opt for an open solution for any other situation, changing origins and destinations, different logger types, and so on.

CONCLUSION

Data management for the pharmaceutical cold chain is a simple concept on the surface. Those who are responsible for managing this important data know that there are many things to consider. It starts with understanding why you are collecting data to begin with and then understanding the best methods for both collection and treatment of that data. Creating a plan of how to manage cold chain data, and to who the responsibility falls, requires an understanding of your goals, challenges and available options. The advent of PDF data loggers has simplified and improved the monitoring process dramatically: they can be configured at the last minute with product-specific profiles (including multi-level-alarm criteria). At the point of destination, they are unpacked and connected to a PC via a standard USB port. The data logger automatically produces a PDF report containing OK/ALARM, alarm statistics and a graph – without any equipment or software needed at destination. As such, the independent PDF data logger is the new generation of cold chain monitoring.

Reference

1. **Assessment of routes and modes of transport is recommended, 61 No S-2: p15, 2007**

About the author

Martin Peter holds a Master of Business Economics from the University of St Gallen, Switzerland. As a Senior Consultant and later as Engagement Manager, Martin has worked in the areas of strategy, process consulting/IT, M&A and cost cutting for a business consultancy focused on travel and transport industry. In 2003 Martin joined Envirotainer as Commercial Manager, and had roles in product development, business development, marketing and sales. As Vice President Sales, he was also member of the Executive Management Team of Envirotainer. In this position he was one of the key drivers behind Envirotainer's transition to become a partner to the pharmaceutical clients and the logistics industry focusing on cold chain management. In 2008 Martin joined ELPRO-BUCHS, Switzerland, as Director of ELPRO's cold chain activities. **Email:** martin.peter@elpro.com