

# Using Technological Advances to Simplify Cold Chain Monitoring Procedures

By Natalie Roy, Product Manager, and James Wilson, Technical Director at Gemini Data Loggers (UK) Ltd



Natalie Roy is a Product Manager at Gemini Data Loggers (UK) Ltd. With over eight years' experience in temperature monitoring and data acquisition systems, she has spent many years with Eurotherm in both the Europe and the US, becoming Data Acquisition Product Manager and principle in-house trainer on 21CFR Part 11 and GAMP for the Americas. Natalie has an MEng in Chemical Engineering from Imperial College and has also studied at the Ecole Nationale Supérieure d'Ingénieurs de Génie Chimique in France.



James Wilson holds an MEng in Electronic Engineering and had been working as an Electronic Design Consultant for a number of years when he first came into contact with Gemini. Specialising in temperature measurement and data acquisition, James joined forces with Gemini's research and development team 10 years ago and is Technical Director for the Gemini group.

With pharmaceutical manufacturers and distributors having to meet the challenges and expense of cold chain distribution under increasingly stringent and far reaching regulations, it's not surprising that there's so much attention being given to the topic within the industry. And yet the Medicines and Healthcare Products Regulatory Agency (MHRA) continues to report worrying figures – 52 per cent of all critical and major deficiencies recorded by the MHRA's good distributions practice (GDP) inspectors during 2002/2003 related to the control and monitoring of storage and transportation temperatures. This represents an increase of 18 per cent over 2001/2002 figures. So where is the industry going wrong?

Part of the problem seems to be industry guidance, or rather the lack thereof. While the pharmaceutical industry is well regulated and legislated, in this area at least, there is a lack of accepted methodology; we know we need to comply with certain regulations, but how do we go about doing it?

## THE CASE FOR ROUTINE TEMPERATURE MONITORING

Already a sea-change can be seen with the widespread adoption of routine shipment monitoring. To date, many manufacturers or distributors have validated their distribution chain but stopped short of measuring the temperature of each shipment. Why bother? While validation of the cold chain is required, it does not in itself guarantee compliant shipments, as there is no verification that parameters remain within the validated limits. The transportation process can never be fully controlled, with challenges to the validated system including temperature extremes, airport handling staff changes (shifts, temporary employees), customs clearing delays (missing/outdated forms, public holidays) and so on. Verification of each shipment with the use of temperature monitoring devices will 'validate' that shipment retrospectively, demonstrate ongoing compliance and allow us to manage variability. Monitoring can supply information on exactly how the goods are treated during every step of the transport process

and can be used for insurance claims, forwarder bench-marking and continuous improvement.

One challenge is to define the extent of routine monitoring required. Data collection should be managed and optimised based on qualification, with enough data to be able to make a judgement on the quality of the goods. But how much is enough?

Happily, guidance is on the way. An industry group called the Cold Chain Committee (3C) is working to define industry-wide, specific guidelines for the receipt, handling and shipping of finished cold chain pharmaceutical products, with a view to obtaining endorsement of these standards from the pharmaceutical industry and regulatory authorities. Already having received much input from manufacturers, the 3C steering committee aims to approach suppliers and authorities by the second half of 2004.

Cold chain guidelines being established by groups such as 3C will make a huge impact on industry understanding and implementation. The benefits of monitoring individual shipments are clear, with adopters seeing a reduction in packaging and courier costs, and the reduction of product loss and associated costs. However, with these benefits comes increased workload in terms of system validation, data retrieval, archiving, and system and data management. Technology improvements will play a central role not only in increasing compliance, but also in driving down the costs of achieving this. Anyone who has worked with 21 CFR Part 11 appreciates that compliance is a mix of technology and procedure. System design advances will enable a reduction in manual procedure, facilitating compliance while driving down the costs associated with traditional shipment monitoring procedures.

While many of the actual data loggers and other devices used in shipment monitoring are perfectly serviceable, the systems built up around them to deal with documentation and data flow (data retrieval, data sharing and archiving) are laborious, costly and open to human error and/or negative intervention. A typical flow diagram for a logger can be seen in Figure 1.

Figure 1: Flow Diagram of Manual Steps for Traditional Shipment Monitoring

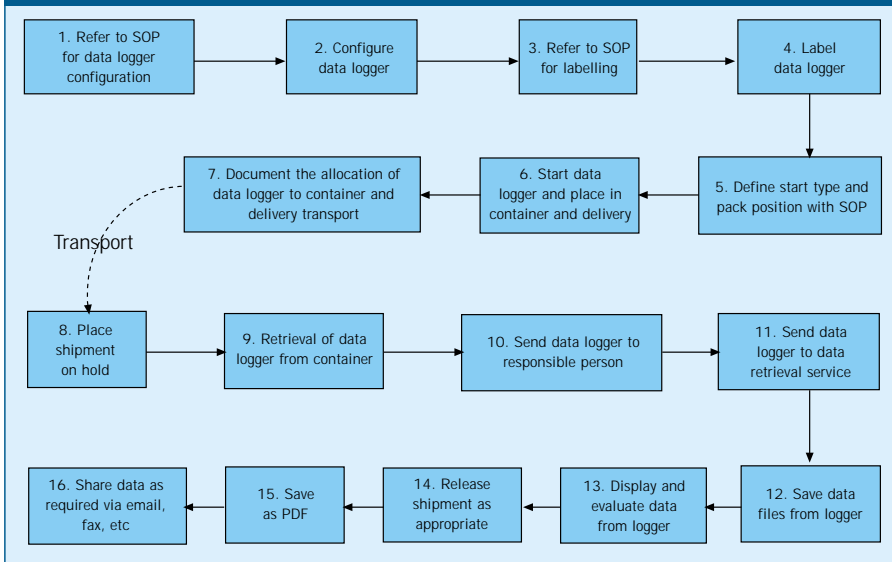
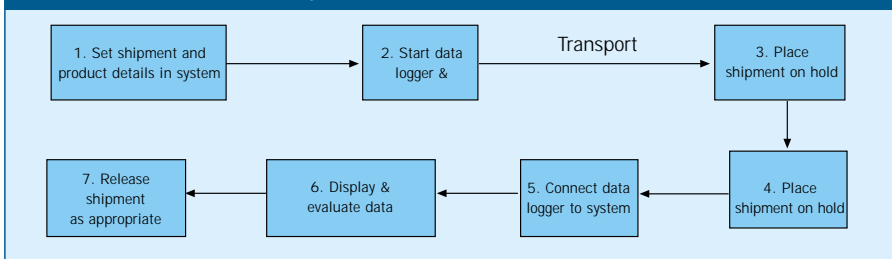


Figure 2: Flow Diagram of Manual Steps for a Centralised Server-Based System Accessed Via the Internet



While much must be done in terms of paperwork at the outbound site linking individual loggers to shipments, the majority of problems occur at the receiving site. Once a shipment is received it is held while data from the loggers is sent to the responsible person (RP) for analysis. The RP is often located back at the originating site or at another site completely. A common method of data transfer in this case is to courier the loggers back to the RP, which increases shipment holding time and is subject in itself to problems. If the loggers are lost in transit to the RP, samples for analysis must be sent back, resulting in more delays and a reduction in product which can be critical for small scale shipments such as clinical trials.

Another method is for data to be extracted on site and data files sent or printouts faxed to the RP. This requires multi-step file handling of possibly sensitive information by the receiving site. It also requires all destination sites to install and run software, have personnel trained in the use of that software and for each computer system to be fully validated.

For both of these methods, the receiving site must follow a multi-step procedure which can be further complicated when shipments have varying RPs and come from varying originating sites.

### OPTIMISATION OF LOGGER PROCEDURES

So how can we keep the benefits of individual shipment monitoring but overcome the associated costs and complexities? How can logger paperwork be dramatically cut, file handling and data transfer be simplified and the need for local software removed? The answers lie in the adoption of a centralised

server-based system that can be accessed from multiple sites via the web. Let's look at how such a system tackles each of the issues we have highlighted in the previous section. In Figure 2 we see a flow diagram for such a system, which should be compared with that of a traditional system in Figure 1.

### Logger Paperwork

All loggers are both launched from and downloaded to the central system, irrespective of their geographical location, through use of the Internet. Because all data is held centrally, shipment and product details (such as delivery address, RP, pallet numbers and stability data) can be associated with the logger electronically in the system, reducing or eliminating much of the paperwork associated with logger monitoring.

### Human Error

On receipt of shipment, the logger is uploaded to the central system. Because the operator performs no file handling

during upload of the logger, confidential data cannot be copied, nor can an operator omit to forward the data file for a shipment release decision.

### Delayed Shipment Release

Downloading data to the central system and making it immediately available to the RP via the Internet removes the delay in shipment release associated with sending the logger back to the RP, or to a logger reading service. Loggers can be collected at the shipment destination and returned in bulk to the manufacturing site for re-use. This has the added benefit of reducing logger courier costs. Adoption of re-useable loggers is environmentally preferable and reduces monitoring costs. This should be of growing consideration with the upcoming European directive on Waste from Electrical and Electronic Equipment (WEEE).

### Logger Loss During Return Journey

A risk of shipping loggers back to the manufacturing site prior to data extraction is that the logger may be lost during return shipment. This usually requires samples of product to be returned for analysis, increasing delays in shipment release and depleting shipped product.

### Data Sharing

Data showing that goods have not suffered negative effects during transport needs to be available at the receiving site (for in-company shipments) and at the supplier site (for external deliveries). Data showing that a transport process is qualified also needs to be available to the supplier. With a server-based model, data is

available immediately on the central system as soon as the logger has been uploaded and data sharing becomes far simpler. Interested parties (defined within the system in the shipment and product details associated with the logger) can receive immediate notification that the shipment has been received, achievable via email/text notification.

#### Data Analysis

The system will check data against product stability data and absolute temperature limits stored within the system before sending out new data notification.

#### Data Sensitivity

Access to uploaded data can be restricted to specific users on a per shipment basis and is password controlled. This model works well for distribution models with third party handling (courier, distributor and end customer) of loggers containing sensitive data. All Internet connections are secure and use https, the same protocol used for secure Internet banking transactions.

#### Software on Third Party Sites

Where a third party (courier, distributor or end customer) is involved in the handling of loggers there may be difficulties with installing and maintaining the logger software on their computers. If a PC is replaced, or a product is re-routed, will there be a PC running software to which the logger can be downloaded? A server-run application accessed via the web does not require any software to be installed locally. A PC with Internet access and a web browser (such as Internet Explorer) is all that is required.

#### System Validation

A single centralised system is easier to validate and control than distributed PCs running installed software with varying network permission models.

#### Additional Benefits

- ◆ Scalability for large distribution models
- ◆ No software roll out costs
- ◆ Central control of procedures
- ◆ Central control of access permissions
- ◆ Central repository of data for analysis and cold chain optimisation

### OUTSOURCING CONSIDERATIONS

With a central system that is accessed via the web, the geographical location of the system becomes arbitrary, opening up the possibility of outsourcing the hosting of the system and all the associated services. Outsourcing can harness expertise that may not exist within the company, for example: data system risk analysis; 21 CFR Part 11 and system validation; data security; and system design for GAMP validation. Outsourcing also has the benefit of fixing the annual cost of your data system, including system and data maintenance. There are several points to consider when outsourcing your cold chain monitoring system to a third party:

- ◆ Operates to quality plan, preferably ISO or equivalent certified

- Carry out a quality audit of the potential service supplier
- ◆ Industry aware
  - Has a sound understanding of GAMP and 21 CFR Part 11
- ◆ The system should specifically be designed to be validated
- ◆ Company will produce risk analyses and functional design specifications
  - These will form the basis of the operational qualification
- ◆ Company will produce system design specification
  - This will form the basis of the installation qualification
- ◆ Security system in place
  - Controlled electronic and physical access to the system
- ◆ Back-up system
  - Mirror servers
  - Off-site storage, which should take into account fire/flood/other disasters
- ◆ The company should have a disaster recovery plan in place for the system

### THE FUTURE OF TEMPERATURE MONITORING OPTIMISATION

With technology improvements already to hand, what will the future bring in terms of the temperature monitoring devices themselves? As with all technology hardware, we'll see the usual trend of reduction in both size and price, but also the adoption of new technology such as RFID. Short for radio frequency identification, RFID uses electromagnetic or electrostatic coupling in the radio frequency portion of the electromagnetic spectrum to transmit signals.

RFID technology has been developing rapidly over the last two years and some of the larger players in the food and retail industries are already adopting a basic form of the technology called electronic product code (EPC), which uses electronic tagging to locate, identify and track objects. Advances in active RFID technology bring the possibility of low-cost data loggers that can record temperature and automatically transmit stored data when passed through a reader gate closer. This cuts out physical handling of the data logger and further simplifies procedures, particularly if data downloads are required at multiple stages during transit.

With clearer guidelines being produced by industry groups, and the progression of technology promising relief from complex and laborious procedures, achieving compliance in cold chain looks to become less of a headache for the pharmaceutical industry. ◆

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Further Information	
Regulations and inspections for the UK market	<a href="http://www.mhra.gov.uk">www.mhra.gov.uk</a>
Regulations for the US market	<a href="http://www.fda.gov">www.fda.gov</a>
GAMP forum	<a href="http://www.ispe.org/gamp">www.ispe.org/gamp</a>
European directive on Waste from Electrical and Electronic Equipment	<a href="http://www.ukonline.gov.uk">www.ukonline.gov.uk</a>
RFID developments	<a href="http://www.appletonideas.com">www.appletonideas.com</a>