



# **Guidance on the interpretation and implementation of European Good Distribution Practice**

## **Chapter 9 – Transportation**

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Pharmaceutical Quality Group of the Chartered Quality Institute**

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## Preface

It is of key importance that medicinal products are not only made to a high quality in accordance with Good Manufacturing Practice, but that the quality and integrity of these products are maintained through the entire supply chain to the patient. This is where Good Distribution Practice (GDP) comes into play.

The distribution network for medicinal products is often complex, involving many different parties. In addition to the challenges associated with this complexity, there is also a growing threat from criminal activities seeking to introduce falsified medicines into the legal supply chain. The European regulators recognised several years ago that there was a need to update the content of the 1994 GDP guideline to take into account advancements in practices and changes in legislation since it was issued. A consultation draft was issued in mid 2011 and, following the receipt of many comments from interested parties, a [final revised version](#) was issued in March 2013 with an effective date of 8 September 2013.

The new guideline has a much stronger focus on the quality system with clear responsibilities and processes and the application of risk management principles. More detailed guidance is given on most elements. New chapters relating to transportation and specific provisions for brokers have been added.

The Pharmaceutical Quality Group issued a monograph on Pharmaceutical Distribution in 1997 and initiated planning to revise this in line with the new regulatory guideline. Whilst undertaking this planning it was identified that the European Compliance Academy were also planning to produce some guidance in response to requests from members. The two organisations therefore decided to join forces and set up a joint steering committee led by Afshin Hosseiny with Philip Butson, Ashley McCraight and Oliver Schmidt.

An early decision was that we would initially target key chapters and issue each as it became available rather than wait until a complete guide had been prepared. This has enabled us to shorten the time to the provision of some guidance and also provides an opportunity for us to collect feedback and enhance the material before issuing a complete guide. The first versions of the chapters will have different formats and styles due to the different volunteer teams involved in their preparation which we have chosen not to edit into a common format for the time being. We would appreciate feedback on what works best for you, the user.

In this document, text from the EMA guideline is given in boxed *italic Calibri* font, followed by guidance from the team in normal Times New Roman font. The main guidance is given in pages 3 – 18 with pages 19 – 32 providing an appendix giving examples of good and poor practices.

Please provide any feedback and suggestions for improvement using the email address [monographs@pqg.org](mailto:monographs@pqg.org) or [info@gmp-compliance.org](mailto:info@gmp-compliance.org).

For this particular chapter on Transportation, we would like to thank the hard work of the authoring team Ciaran Brady, Kane Edgeworth, Patrick Grey, Margaret Murphy and Tatjana Vorobiova. Additional material was provided by Afshin Hosseiny and editing was undertaken by Philip Butson, Afshin Hosseiny and Ashley McCraight.

**See Appendix for Good and Poor Practice and some additional information.**

### **9.1. Principle**

*It is the responsibility of the supplying wholesale distributor to protect medicinal products against breakage, adulteration and theft and to ensure that temperature conditions are maintained within acceptable limits during transport.*

*Regardless of the mode of transport, it should be possible to demonstrate that the medicines have not been exposed to conditions that may compromise their quality and integrity. A risk-based approach should be utilised when planning transportation.*

### **Definition/Clarification**

The licensed supplier of the medicinal products (e.g. a wholesaler or manufacturer) must ensure that products are transported so that they are received by the intended recipient 'fit for use'. The supply chain must have adequate security to prevent theft of product and minimise the risk of falsified products entering the supply chain. The chosen route of transportation must ensure that the products are maintained within their required temperature parameters at all times. Documented evidence must be kept and be available, showing the supply chain route that the products were distributed through and the conditions that they were exposed to during transportation. This could be demonstrated with temperature monitoring in vehicles, data loggers included in the shipment or previous qualification of the transportation route (taking into account seasonal variations). All distribution of medicinal products must be based on risk and documented accordingly, for example, taking into account the type of product and required storage conditions, journey time, method of travel (road, sea, air), time of year and expected external conditions.

### **Benefits**

Ensure that only medicinal products that are fit for use are supplied to patients. Poor storage/distribution conditions can affect the efficacy of a medicinal product resulting in the medication not having the desired effect on the patient.

Falsification of medicines is an increasing issue on the worldwide pharmaceutical market and results in sub-standard products being taken by patients across the world, creating a risk to public health. Everyone involved in the pharmaceutical supply chain has a responsibility to ensure only genuine products make it to patient level, having a robust and secure supply chain is one way of ensuring this.

### **Risks**

Not having a secure, risk-based supply chain can result in sub-standard products being sold and prescribed. If a product has particular storage requirements such as +2°C to +8°C, these conditions must be maintained so the product continues to meet the requirements of its licence. Temperatures outside of this range will affect the efficacy of the product.

## 9.2 Transportation

### 9.2.1

*The required storage conditions for medicinal products should be maintained during transportation within the defined limits as described by the manufacturers or on the outer packaging.*

Wholesalers and/or manufacturers should be responsible for specifying the actual label claim on the outer packaging and in advance when shipping/transporting/distributing product. Any appropriate temperature or special conditions required should be requested when booking transportation and planning delivery routes. These delivery modes can include air, sea, road and a mixture of any or all of these, for single or multiple shipments.

Normally, the manufacturer has responsibility to the Distribution/Wholesaler and the Distribution/Wholesaler then takes over responsibility to final delivery point.

The IATA label is recommended for time and temperature sensitive products (see link below for more information).

<http://www.iata.org/whatwedo/cargo/pharma/Pages/ttlabel-faq.aspx>

### Benefits

If storage conditions are clearly described on the outer packaging/labelling, all stakeholders can ensure compliance during transportation and storage.

### Risks

If storage conditions are not visible, patient safety could be compromised.

### 9.2.2

*If a deviation such as temperature excursion or product damage has occurred during transportation, this should be reported to the distributor and recipient of the affected medicinal products. A procedure should also be in place for investigating and handling temperature excursions.*

A temperature excursion is a deviation from the labelled storage conditions of a product for any duration of time whether during storage or transportation. All excursions should be successfully managed under a Quality Management System and as per the detailed specifications in your Technical Agreements.

Corrective actions should be identified and implemented following the investigation of any deviation in order to prevent recurrence.

### 9.2.3

*It is the responsibility of the wholesale distributor to ensure that vehicles and equipment used to distribute, store or handle medicinal products are suitable for their use and appropriately equipped to prevent exposure of the products to conditions that could affect their quality and packaging integrity.*

### 9.2.4

*There should be written procedures in place for the operation and maintenance of all vehicles and equipment involved in the distribution process, including cleaning and safety precautions.*

### 9.2.5

*Risk assessment of delivery routes should be used to determine where temperature controls are required. Equipment used for temperature monitoring during transport within vehicles and/or containers, should be maintained and calibrated at regular intervals at least once a year.*

*See sections 9.3.2 and 9.4.4 for more detail.*

### 9.2.6

*Dedicated vehicles and equipment should be used, where possible, when handling medicinal products. Where non- dedicated vehicles and equipment are used procedures should be in place to ensure that the quality of the medicinal product will not be compromised.*

### **Covering 9.2.5 & 9.2.6 - What is a dedicated vehicle?**

A dedicated vehicle is one which is used to transport medicinal product only. Normally it will contain one customer's/supplier's product or consignment. It will normally travel from an approved, authorised site to the approved final delivery point under controlled procedural processes.

Some pharmaceutical companies, for example, are using dedicated vehicles to pick up medicinal products from two or more manufacturing sites and deliver to, a number of approved delivery points. It is essential to ensure the sharing is based on a risk management approach. E.g. if transporting APIs and finished product, compatibility must be carefully established.

Most likely the dedicated vehicle will be of solid side construction on air ride suspension, with rear opening doors which will be locked/sealed. This vehicle will be fitted with appropriate calibrated temperature controlled equipment and most likely GPS tracked, using a GDP trained driver. The company used to supply the vehicle and driver will be an approved transportation supplier. . A Contract/Technical Agreement should be in place with the supplier who will be approved under appropriate QMS standards, procedures etc. The vehicle will be well maintained, clean (with records) and suitable for medicinal products or materials

transportation. This should include for example annual re-calibration on/before the due date, breakdown contract and documented records.

### **What is a non-dedicated vehicle?**

A non-dedicated vehicle is one that will carry medicinal product as well as non-medicinal product /materials on the same vehicle.

Risks associated with non-dedicated vehicles are that medicinal products could be loaded with other medicinal products or indeed any other types of product, e.g. Agricultural, chemicals, food, flowers etc. These other products may be packed on pallets or loose cartons/drums, destined for multiple delivery locations. Untrained and/or unapproved transport contractors and sub-contractors might be used.

Non-dedicated vehicles used for collections (and deliveries) will require procedural controls and processes that can demonstrate distribution compliance based on risk. These should be supported by very good contracts with responsibilities/accountability clearly defined.

### **Benefits of using dedicated vehicles**

Dedicated vehicles reduce the risk of cross-contamination and are more likely to provide a safe, secure and traceable method of transporting medicinal product within a controlled delivery process.

#### **9.2.7**

*Deliveries should be made to the address stated on the delivery note and into the care or the premises of the consignee. Medicinal products should not be left on alternative premises.*

### **Delivery note Definition/clarification:**

Delivery note is the document containing, but not limited to, full delivery address (including consignee details and telephone number); customer name; protocol name; carrier details; description and quantity of the product; shipping and storage conditions for the product.

Examples of documentation included in delivery note are: packing list; airway bill; manual order form; Proforma invoice.

All deliveries should be accounted for and have a POD (proof of delivery - usually retained by a carrier) available. Date, time, consignee name and signature should be documented upon each delivery.

Deliveries of medical products considered hand-to-hand service specific to the consignee indicated on the delivery note, therefore at no time should medical products be left on alternative premises.

## Benefits

Medical products are delivered right the first time, to the correct consignee within the assigned timeframe.

Temperature conditions of the medical products are adhered to up to the point of the final delivery.

Medical products are handed into the possession of trained personnel and a final consignee (who are able to stop temperature monitors if needed and record temperature parameters appropriately).

Drivers who are GDP trained will know the critical importance of documentation and especially collection, delivery and PODs.

## Risks

Medical products left unattended may be lost and a POD may not be available.

Medical products delivered to an alternative consignee may be stored incorrectly.

Medical products delivered to alternative premises may be misused.

### 9.2.8

*For emergency deliveries outside normal business hours, persons should be designated and written procedures should be available.*

## Definition/Clarification

**Emergency delivery** may be defined as a situation where medical products need to be delivered or picked up immediately for 'last minute' product needs (usually within a 24-hour window).

**Specialist carrier** (premium service provider) will usually be utilised for outside normal business hours (9am-5pm). They provide 24/7 global service via the normal operations telephone numbers and e-mail. Contact number/person, mobile for out of hours' contact, to be provided at the consignee site for all deliveries.

Carriers should have SOPs (Standard Operating procedures) set out for contingencies such as this, which will include contact numbers, address and details to successfully deliver the product/consignment with trained drivers. SOPs for emergency deliveries should also be available.

## Benefits

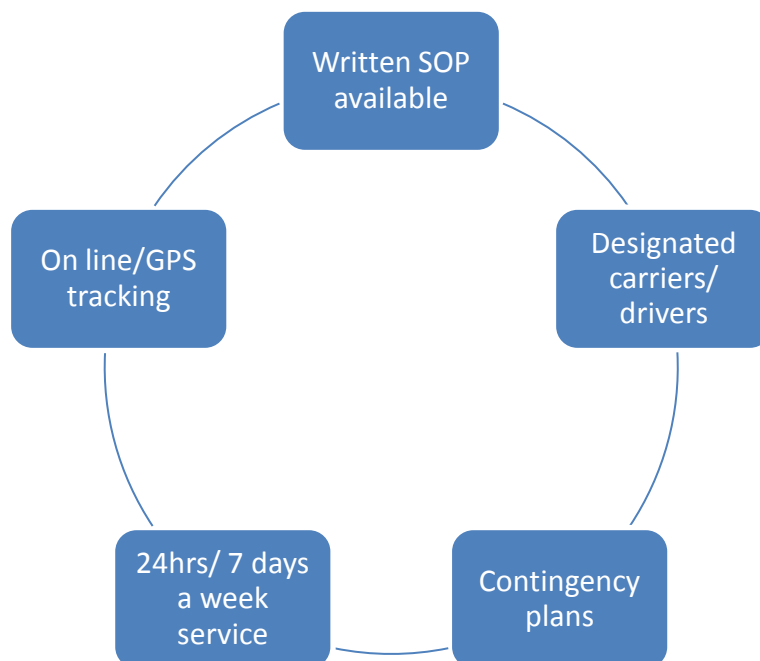
- 100% on-time deliveries.

- Use of specialist courier ensures online tracking; GPS tracking; performance reports availability; proactive notification of issues.
- Exceptional customer service.
- Contingency plans available.
- Ensure patients receive medication in emergency situations.

## Risks

Medical products are not delivered on time for emergencies which places patients at risk!

## Check/list:



### 9.2.9 (a)

*Where transportation is performed by a third party, the contract in place should encompass the requirements of Chapter 7. Transportation providers should be made aware by the wholesale distributor of the relevant transport conditions applicable to the consignment. Where the transportation route includes unloading and reloading or transit storage at a transportation hub, particular attention should be paid to temperature monitoring, cleanliness and the security of any intermediate storage facilities.*

## The contract

A contract is a written agreement between two or more parties which creates obligations that are enforceable by law. Before services are provided by a vendor, a contract must be put in place and executed by the parties. Examples of contracts include, but are not limited to, Service Provider Agreements, Master Services Agreements and Consulting Agreements.



The contract should detail the required mode of transportation and relevant transport conditions. Transportation providers (carriers) should be informed by a wholesale distributor of the relevant transport conditions at the point of scheduling the collection/pick up, usually via web based systems or telephone/e-mail communication.

Transportation providers must have SOPs/document procedures for temperature and environment monitoring of the temporary storage of the drug products.

Procedure may include, but not limited to, recovery of customs/flight delayed shipments to an appropriate controlled storage facility which can be an airline facility at the airport involved, repacking into freshly conditioned validated packaging, dry ice replenishment and has on occasion involved collecting in a refrigerated vehicle for delivery.

Carrier must also complete relevant inspection/audit of the temporary storage facilities. Checks should include for example checks on temperature monitoring, cleanliness and security of any intermediate storage facilities.

Security procedures for imports/exports should also be utilised by transportation providers.

This may consist of documented cargo inspections before, during and after the transportation. In some instances, predetermined routes should be identified which are subject to further inspections to verify length and time between loading point and collection; customs border; delivery destinations etc.

#### **Check/list:**



#### **9.2.9 (b)**

*Provision should be made to minimise the duration of temporary storage while awaiting the next stage of the transportation route.*

The following provisions may be utilised:

Pre-clearance of the shipments where possible.

To minimise any transit or customs delays (which could result in temporary storage), careful planning must take place prior to despatch of the shipment: pre-submission of the shipping/customs documents to relevant Health authorities/Customs to gain approvals. No shipments, especially temperature sensitive, must be despatched until approvals are received.

Checks for valid import licences and/or relevant health authorities' authorisations must be made.

Transit delays involving temporary storage must be always treated as urgent. Alternatives (next flights, pick up by a refrigerated vehicle, etc.) must be investigated and utilised as a priority in all cases.

### **Clarification/Definition**

The traditional 48-hour rule to move to the next stage of transportation in a carefully planned well managed supply chain could still be used where possible. Of course, the type of product using a risk based approach should be carefully considered for both planned and unplanned events.

If your supply chain is mapped you should understand all touch points including the use of air, sea, road and a mixture of unloading and reloading hubs, warehouses/touch points. Most likely they will have received audits and be approved for use with written contracts/agreements in place to ensure best practice for product protection, safety, security, quality and compliance. Records should be available for all durations of temporary storage.

Guidance on when temporary storage facilities are required to be licensed is not harmonised across Europe and it is important that companies are aware of, and comply with, national regulatory expectations.

Supply chains should be mapped to identify stop over and hand over locations and risks assessed and documented. Where identified by risk assessment, these locations should be audited. Other risk mitigations might include temperature monitoring and vehicle security arrangements, for example.

The 'owner' (title holder) of the product should be responsible for mapping the shipment route to the next party in the supply chain.

### **Benefits**

Minimise any transit or/and customs delays.

By ensuring all shipment documentation is up to date, shipments will not be held up or searched.

If you have approved temporary storage facilities it will provide greater assurance that they are suitable for your product.

### **Risks**

Medical products are not delivered on time or temperature conditions are not adhered to at the temporary storage.

Possibility of theft at the temporary storage and falsified medicines entering the supply chain.

### **9.3. Containers, packaging and labelling**

#### **9.3.1**

*Medicinal products should be transported in containers that have no adverse effect on the quality of the products, and that offer adequate protection from external influences, including contamination.*

(See after 9.3.2 for Definition; See Appendix for Good Practice and Poor Practice).

#### **9.3.2**

*Selection of a container and packaging should be based on the storage and transportation requirements of the medicinal products; the space required for the amount of medicines; the anticipated external temperature extremes; the estimated maximum time for transportation including transit storage at customs; the qualification status of the packaging and the validation status of the shipping containers.*

Storage conditions on product labels are based on stability data submitted as part of the Marketing Authorisation Application. Marketing Authorisation holders may specify shipping conditions, but in the absence of any other conditions being specified, the labelled storage conditions should be maintained and any deviations from these referred back to the Marketing Authorisation holder for assessment.

- Shipping studies are useful in documenting temperatures from the outside of packages to the chosen destinations. Multiple dummy shipments sent through chosen lanes should be carried out during the seasonal extremes at both ends of the supply chain. Studies should be designed to capture any trends or issues during transit and can take a lot of the guess work out of the temperatures that product or packages will be exposed to during transit. The study results will provide accurate detail to justify the selection of packaging and containers. Your freight-forwarder or logistics company can be an important partner in supporting this process and improving the efficiency of capturing the data. Providing regular updates to them can also be a useful exercise and make it easier to investigate any issues as well as show the positives.
- Off the shelf or bespoke packaging solutions are available and can be supplied with validation packages that might suit more than one destination and product type or size. Validation packages should be assessed for suitability and also include sufficient protection against unforeseen circumstances such as flight and customs delays.
- Some controlled packaging solutions are reusable but the cost feasibility of returning the boxes should be assessed and SOPs put in place to monitor the packages for damage and number of suggested uses.

Consideration should be given for the storage and transportation of medicinal products. *See Appendix, section 9.3.2 for examples.*

Shipping studies can remove a lot of the guess work from the potential conditions that products/packages will be exposed to during transit.

Shipping studies can also be a valuable exercise when a packaging/shipment lane is already in place but is perhaps giving issues. The data can be used to justify/update procedural changes or product/service selection.

### 9.3.3

*Containers should bear labels providing sufficient information on handling and storage requirements and precautions to ensure that the products are properly handled and secured at all times. The containers should enable identification of the contents of the containers and the source.*

Below covers 9.3.1 and 9.3.3:

### **Definition/Clarification**

A shipping container is the vessel that is used to transport a product. It could be a lorry, van, reefer, 20ft / 40ft steel container or active temperature control boxes.

The packaging is the carton or box that the product is placed in for transportation. It could be a cardboard carton, validated insulated shipper, tote box etc.

Labelling is referring to the shipment labels and not the actual product labelling. All shipments of medicinal products should bear labels showing the type of product, the required temperature conditions and any special handling requirements.

### **Benefits**

Choosing the correct shipping container and/or packaging and applying the appropriate labels is essential for ensuring that medicinal products are received at the intended destination fit for use.

### **Risks**

Without assessing the appropriate shipping container or packaging for a product, it is likely that the product will be subjected to temperature conditions that could adversely impact on the efficacy of the product, and without labelling to identify the required shipping and handling conditions, the wrong transportation method could easily be used in error, even if the supplier has assessed what the appropriate method of transportation should be.

## 9.4 Products requiring special conditions

### 9.4.1

*In relation to deliveries containing medicinal products requiring special conditions such as narcotics or psychotropic substances, the wholesale distributor should maintain a safe and secure supply chain for these products in accordance with requirements laid down by the Member States concerned. There should be additional control systems in place for delivery of these products. There should be a protocol to address the occurrence of any theft.*

### 9.4.2

*Medicinal products comprising highly active and radioactive materials should be transported in safe, dedicated and secure containers and vehicles. The relevant safety measures should be in accordance with international agreements and national legislation.*

## 9.4.1 & 9.4.2

### **Definition/Clarifications**

As stated in this chapter over a number of sections, a safe secure supply chain must be planned and carefully managed to meet the specific conditions based on the product requirements.

Products such as narcotics, radioactive or psychotropic substances must be managed under procedures that will ensure national and international safety measures are in accordance with best practice as you source, store, transport and deliver these products.

### **Benefits**

By having good procedures and well trained competent and experienced staff managing these products across the supply they will be aware of the risks and ensure a tried and tested system will deliver compliance. Any theft or issues must be covered in agreements and it must be stated clearly who has responsibilities to address these. Processes and protocols should be in place to manage such events successfully in a timely fashion at the correct level in all organisations managing the supply chain.

### **Risks**

These products are often watched carefully along supply chains and can be stolen by people that don't have patient safety or quality at the top of their agenda.

#### 9.4.3

*For temperature-sensitive products, qualified equipment (e.g. thermal packaging, temperature-controlled containers or temperature controlled vehicles) should be used to ensure correct transport conditions are maintained between the manufacturer, wholesale distributor and customer.*

Active or passive packaging solutions can be considered as well as temperature controlled vehicles:

‘Off the shelf’ validation packages (if available) are often suitable but if not sufficient, a more expansive qualification exercise may be required to prove suitability of solution, for example the thermal profile used needs to replicate the intended worse case temperature exposure expected.

Packaging qualification exercises:

- Min/Max Loads
- Tailored thermal profiles representing required seasonal extremes (climatic chamber profiles (based upon ISTA procedure 7D (2007))). Profile choice should reflect extremes of temperature at shipping & receiving locations.
- Build in worst-case test times to take into account transit delays such as customs
- Vibration and compression testing can also be useful to include if required

On-going monitoring programmes (data logger position and placement density) should be based upon the mapping exercise or qualification of the shipment method.

Having a robust approach to qualification will provide the proof of suitability to both the regulator and the client. Completing properly documented mapping and qualification exercises shows suitability of use for a chosen purpose and provides the best possible chance of product being transported in the correct conditions. (Details on vehicle mapping can be seen in Appendix, Section 9.4.4).

#### 9.4.4

*If temperature-controlled vehicles are used, the temperature monitoring equipment used during transport should be maintained and calibrated at regular intervals. Temperature mapping under representative conditions should be carried out and should take into account seasonal variations.*

#### **Calibration**

Equipment critical to assuring the quality of product should be calibrated according to written procedures and an established schedule as stated in section 5.3 of the Good Manufacturing Practice (GMP) guidelines (Part II: Basic requirements for Active Substances used as Starting Materials). A minimum 12 month calibration interval is often chosen as the industry standard.

Section ‘3.3 Equipment’ of this document also refers to calibration and states a requirement for equipment to be calibrated at defined intervals based upon a risk and reliability assessment.

Probes should be calibrated to traceable National or International Standards, such as UKAS (United Kingdom Accreditation Service) or NIST (National Institute of Standards & Technology), over the operating range.

### **Mapping**

Vehicle mapping should be carried out in Summer & Winter conditions and repeated according to the results of a documented risk assessment or whenever significant modifications are made to the temperature controlling equipment or vehicle.

*See Appendix Section 9.4.4 for more detail.*

#### **9.4.5**

*If requested, customers should be provided with information to demonstrate that products have complied with the temperature storage conditions.*

Vehicle prints should be signed and archived but consideration given to:

- Vehicle prints not always sufficient due to CMPs not being at product level (often situated at top of the vehicle above the load limit line)
- Vehicle print hard copies can degrade over time and become unreadable – scanned electronic copies will provide permanent archive option

In order to prove suitable temperatures have been maintained it is advisable to have a temperature monitoring programme in place where data loggers are placed at product level during each shipment.

Temperature monitoring data should be assessed for each shipment and regularly reviewed for any trends in location/route failures.

If reliance is placed on the data from the vehicle temperature logger, then it should be assured that the location of the temperature probe ensures the data are representative of the product temperature since there can be variation throughout the container.

Data loggers are now widely available, accurate and relatively inexpensive providing proof of conditions during transit. A small investment in respect to the high value of medicinal products in temperature monitoring during transit can provide valuable data for general product release and proof of condition, especially in cases where notable events have occurred in transit that could have compromised product temperature such as doors being left open or product being left outside for periods of time during loading & unloading procedures. In reality when pallets/containers are being transferred from one controlled zone to another they will often be outside the specified temperature range. E.g. they may be at ambient conditions. This should be minimised and there should be understanding of the criticality for each of the products handled. This is particularly important for vaccine products. The

situation can be controlled by setting a cumulative limit for ‘Time at ambient temperature’ (TAT), which is based on stability evidence and defined in technical agreements. Where there are excursions from this agreed TAT, advice should be sought from the Marketing Authorisation holder.

#### 9.4.6

*If cool packs are used in insulated boxes, they need to be located such that the product does not come in direct contact with the cool pack. Staff must be trained on the procedures for assembly of the insulated boxes (seasonal configurations) and on the reuse of cool packs.*

#### Definition/Clarification

This requirement is for the use of insulated boxes using passive cooling to maintain the product temperature, usually between +2°C to +8°C if cool packs are being used. In this context the cool pack is likely to be frozen. It is important to ensure that cool packs do not come into direct contact with the actual product being packed as this may result in localised freezing of the medicine. An SOP and diagram should be available detailing the packaging configuration for the insulated boxes in line with the validation (as described in section 9.4.3) of the box. The SOP should also include the process for freezing the cool packs and potential reuse of cool packs. All personnel involved in the packing of the insulated should be trained in this SOP.

#### Additional Clarification:

*Although this section mentions cool packs, this section is also valid for controlled room temperature products, where the use of ‘warm packs’ are used instead of cool packs.*

*Examples of Cool pack used for product transport:*



#### Benefits

Insulated boxes are an efficient method of transporting temperature sensitive products usually in small to medium quantities. It is essential that the boxes are packed in accordance with a validation study that has identified a packing specification that will maintain the required temperature for the required journey time.



## Risks

Not having these processes documented and trained to personnel will result in varying levels of temperature excursions to the packed products:

Due to insulated boxes being a passive cooling system, they are significantly influenced by the external temperatures surrounding them. Using a packing specification validated for the summer months (when external temperatures of +15°C to +25°C are expected) during winter when temperatures around 0°C are observed in uncontrolled ambient vehicles, will increase the risk of freezing the product. Alternatively, if using a winter packing specification during the summer is likely to result in the required temperature not being maintained for long enough.

If there isn't adequate insulation and/or spacing between the cool packs and the product when packing an insulated box, it can lead to the product being subjected to temperatures outside of the required conditions (in this context below 2°C).

To minimise cost of packaging, it is possible to reuse some types of insulated packaging and cool packs (however always follow manufacturer recommendations). When this is appropriate, the boxes and cool packs must be checked by trained personnel for any damage which could impact the effectiveness and safety of the box. For example, checks for cracks, dents, holes etc. in the insulated box, and leaks or signs of leakage with the cool packs. If signed off for reuse, cool packs must be reacclimatised to the required temperature for the required amount of time, as defined by the validation.

Without a process in place for the reuse of cool packs and insulated boxes, it is likely that the products temperature requirements will not be maintained. Damaged insulated boxes will result in a change to their insulation properties and therefore a change to the timescale that the required temperature will be maintained. Damage to the cool packs could result in less cooling energy within the box leading to a shorter validation time, and leakage could also contaminate the product. It is important for the reused cool packs to be reacclimatised at the correct temperature for the required amount of time (as defined by the validated packing specification) in order for the product to remain at the required temperature for the entire journey

### 9.4.7

*There should be a system in place to control the reuse of cool packs to ensure that incompletely cooled packs are not used in error. There should be adequate physical segregation between frozen and chilled ice packs.*

## Definition/Clarification

A process must be defined and documented which describes the use and reuse of cool packs with regard to freezing them. All cool packs will have a minimum amount of time that they must be acclimatised for before packed in an insulated container, so the process must detail

how this is ensured. Fully and part frozen cool packs must be clearly segregated so only cool packs which have been acclimatised for the validated time period are used.

### **Benefits**

Cool packs will maintain the required temperature in line with the validation performed and will minimise the risk of the product being subjected to a temperature excursion.

### **Risks**

It is important for the reused cool packs to be reacclimatised at the correct temperature for the required amount of time. Ice packs too cold can result in freezing the product and ice packs too warm or not acclimatised for long enough will result in the required temperature not being maintained for the full validation period. Without adequate segregation between fully and partly acclimatised cool packs, the risk of using insufficiently frozen cool packs is increased.

#### **9.4.8**

*The process for delivery of sensitive products and control of seasonal temperature variations should be described in a written procedure.*

### **Definition/Clarification**

Seasonal temperature variations can have a huge impact on the distribution of temperature sensitive products. For example, temperatures in Southern Europe or the Middle East can reach 50°C in summer months and in Northern Europe and Northern America temperatures drop below -20°C during winter. This can have a great effect on the temperature of a vehicle or insulated container. A procedure should be written to identify the different shipping methods used to counteract the seasonal temperature variations. Refer to the MA for correct storage conditions

### **Benefits**

By having a documented process for defining the shipping the methods to be used for temperature sensitive products during seasonal variations, it will minimise the risk of temperature excursions during transportation.

### **Risks**

If no attention is paid to seasonal temperature variations, the risk of temperature excursions will increase dramatically. An insulated container with a packaging configuration validated at external temperatures of 15°C to 30°C (suitable for summer shipments), being used to ship 2°C to 8°C product, is likely to freeze the product if being transported on an uncontrolled vehicle in the middle of winter. Alternatively, an uncontrolled vehicle could be suitable for transporting an ambient product requiring storage at less than 40°C, but if the same product has a storage requirement of 'Do Not Refrigerate', an uncontrolled vehicle in the middle of winter would not be acceptable.

## ***Appendix: Transportation Chapter 9 – Good and Poor Practice examples***

### **9.1**

#### **Good Practice**

A Risk Based Approach:

Know the products being supplied:

What are the storage requirements? Does the manufacturer make any further recommendations? What quantity is being shipped?

Know the Supply Chain:

What is the distance of the journey? What routes are to be taken? Which modes of transport are required? What is expected journey time? What are expected conditions (Northern Germany in January, South of France in July)

Are there any points in the supply chain where delays can be anticipated, e.g. countries with a history of customs delays?

Use this information to conduct and document a risk assessment to determine the appropriate transportation route and equipment required.

### Risk Assessment Example

Product	Storage Condition	External Environment conditions	Storage Risk Rating	Environmental Risk Rating	Overall Product Risk Rating	Duration of Journey	Vehicle	Overall shipment risk rating
Example	2°C - 8°C	28 °C	3	3	9	2	3	54

#### Storage condition risk rating is defined as:

0°C -30°C = 1

15°C -25°C = 2

2°C -8°C = 3

#### External Environment risk rating is defined as:

Winter (2- 10 °C ) = 1

Spring/Autumn (10 – 20 °C ) = 2

Summer (>20 °C ) = 3

#### Duration of Journey risk rating is defined as:

1– 5 hrs = 1

5 – 15 hrs = 2

>15 hrs = 3

#### Overall risk rating:

0-10 = very low risk

11-25 = low risk

26-40 = medium risk

41-65 = high risk

66-75 = very high risk

What a secure supply chain should include:

Vehicles should include the following:

Solid sided vehicles, secure locking mechanisms, recorded security seals, GPS tracked, possibly temperature controlled.

Transit Hubs should be sound, secure and clean. Risk assessments and ideally audits should be conducted where compliant transit hubs are not used. Good practice would include such controls as CCTV, intruder alarms, security, locked doors/access control and a fenced site.

Personnel should be GDP-trained, process trained, experienced and competent. GDP

Awareness training should cover all supply chain staff for example, office staff, warehouse staff, facility staff including touch points/temporary storage locations and drivers.

### **Poor Practice**

Examples:

Using curtain sided vehicles for high value, temperature sensitive products.

Shipping +15°C to +25°C product in standard shipping container during summer or winter without data loggers.

Shipping medicinal products with unapproved Groupage (see sections 9.2.5 and 9.2.6; non-dedicated vehicles are normally called Groupage.)

Shipping +2°C to +8°C and +15°C to +25°C product in the same temperature compartment on a vehicle to reduce cost. Each should be in their appropriate temperature compartment.

#### **9.2.1**

### **Good Practice**

As supply chains are becoming more complex and falsified medicines continue to be a significant risk, understanding your supply chain is essential for successful management under GDP.

All wholesalers/manufacturers should map out their whole supply chain and know what controls are in place for temperature, humidity, security and risk of cross contamination at each stage of transportation. This should include the use of all temporary storage locations, hubs, etc. All locations should be approved and audited against specific storage/transportation standards and requirements. See also section 9.2.9(b)

The type of product (e.g. cold chain, narcotics) must be carefully considered to ensure storage and security in the transportation process.

**Poor Practice**

Product is shipped without labelling specifying product temperature or storage requirements, through an unapproved supply chain.

Product is left in temporary locations where product integrity, security and compliance are not safeguarded, putting patients and products at risk.

If unsuitable transit/temporary locations are used, product compliance could be compromised.

**9.2.2****Good Practice:**

Temperature excursions (including extent and duration) should be notified immediately (as per Technical Agreement terms) to the Responsible Person or the Wholesaler or Qualified Person in the Manufacture or the recipient of the affected medicinal product in a timely fashion and recorded.

A detailed procedure should be in place for investigating, handling and managing all temperature excursions including during transportation. Notification of key stakeholders and careful management of the product is also essential.

All temperature monitoring records should be regularly reviewed and approved to ascertain whether an excursion may have occurred and a full investigation should be performed and documented including the outcome and notification to all key stakeholders. This should include a review and sign-off of a physical or electronic temperature printout/output from a vehicle to ensure compliance.

Any products stored or transported that are subject to a temperature excursion should be quarantined in a secure area until the outcome of the investigation is known and the wholesaler, manufacturer/marketing authorisation holder should be consulted to ascertain whether any possible product quality impact may result from the excursion.

The management of temperature excursions should be described within a procedure and Technical Agreements, which will include any 3rd parties who have responsibilities in the supply chain e.g. transportation companies, 3rd party storage locations/wholesalers.

**Poor Practice**

Wholesaler shipped a cold chain product to a customer. The product was received and signed at goods in, as staff verified that the temperatures printout showed all temperatures during the journey were between 2°C and 8°C. When the first box was opened an ice pack had come in contact with the product and the product was frozen on inspection. The product was rejected. The protocol for packing the products was not followed, as it clearly indicated that the ice pack should never come into contact with the product.

### 9.2.3 & 9.2.4

#### **Good Practice**

Covering points 9.2.3 and 9.2.4.

Use of dedicated transportation and equipment to ensure vehicles/equipment used to store, handle and distribute products using approved transport companies and trained drivers should ensure quality and timely delivery of products. Quality of packaging, integrity and suitability of materials should be tested to ensure no breakage or damage in normal transportation modes.

All transportation companies under the terms and conditions of contract (see Chapter 7) should be approved (and ideally audited) to ensure that procedures are in place which demonstrate, for example, all maintenance, calibrations, cleaning and safety records of equipment used in the distribution process, so product quality is unaffected.

All approved transport companies used should be listed on your Approved Vendor/Supplier Master List.

#### **Poor practice**

Recently a truck was loaded with 3 pallets of temperature sensitive products and the loading took place on a Saturday morning, when the usual GDP trained staff were not working. The load was rejected on Tuesday when it arrived in Europe because goods were contaminated.

### 9.2.5 & 9.2.6

#### **Good Practice**

Use of the correct vehicles and equipment, and approved suppliers will ensure products are delivered within compliance.

#### **Poor Practice**

Use of a non-dedicated vehicle in which a strong-smelling chemical was also transported can lead to tainting of the medicinal products.

### 9.2.7

#### **Good practice:**

Medical products should be delivered strictly to the address noted on the delivery note.

All deliveries must be made precisely to the consignee noted on the delivery note. No alternative consignee should be selected unless it was agreed and approved in advance with the supplier (manufacturer, wholesaler, etc.) and the receiving site.

In some instances, a specific time slot for receiving the delivery may be agreed up-front with the receiving site and should be adhered to by the carrier. Site must be informed of any transit

delays if they happen, otherwise for next-day-only deliveries, carrier must attempt to deliver medical products before 12pm each day or as in the conditions of contract.

Drivers must record exact time of delivery and consignee details and signatures to ensure good POD (Proof of Delivery) process.

#### **Poor Practice**

A medical product delivery was left at the reception as consignee was not available at the time. The receptionist was off duty on that day and no one took notice of the delivery. As supplies were temperature controlled, by the time they were handed into the possession of final consignee, supplies were passed the assigned validation period.

#### 9.2.8

##### **Good practice:**

For any emergency deliveries use of a specialist carrier is necessary. For the deliveries outside normal business hours, an SOP must be in place defining the following:

They provide 24/7 global service via the normal operations telephone numbers and e-mail.

Contact number/person, mobile for out-of-hours contact, to be provided at the consignee site for all deliveries.

Use of appropriately GDP trained drivers only.

Online/GPS 24/7 tracking.

Contingency plans (for example, track by road if flight was cancelled and no further flights available).

##### **Poor Practice:**

Standard courier is used for emergency deliveries which cannot guarantee delivery at the required day/time. E.g. A lifesaving drug had an emergency delivery planned for a Friday at 3.30pm. The product was not delivered until Saturday morning. This is totally unacceptable as it puts the patient at significant risk.

No SOP in place; no GDP trained drivers & no contingency plans.

#### 9.2.9. (a)

##### **Good practice:**

A written contract/s must be in place between transportation company/carrier (Contract Acceptor) and the Wholesaler or manufactures (Contract Giver) before services can commence.



Determined effort to establish effective and reliable communication channels between all parties in the supply chain is a general good practice.

Specifically in relation to the minimisation of duration of temporary storage, web-based tracking systems may be useful to flag and resolve potential or actual problems. As an example, a site shipment to France was collected by a carrier from the wholesaler on Friday. There was an airline strike in France taking place. Since the wholesaler had already alerted the carrier via a web-based system on the upcoming shipment as part of their contractual obligation, the carrier made alternative arrangements to route the shipment via road hence avoiding delays by air.

**Poor practice:**

A medical product shipment was stopped at customs due to customs officer requiring further documentation. The shipment was time and temperature sensitive. Customs clearance took longer than anticipated and as a result the period for which the shipper was validated to maintain storage conditions was exceeded. Appropriate arrangements had not been made to match the validation of the shipper with the potential for customs delays.

9.2.9 (b)

**Good Practice**

If you plan and map your supply chain there should be no surprises in any facilities used for temporary storage. GPS and track-and-trace techniques should be used to manage the movement of your products. Devices are now available that can be placed on a pallet or individual box so you will always know where your product actually is at any point in time.

Where possible, use licenced sites that have successfully passed regulatory inspections for temporary storage. These sites will ensure under their Quality Management System a safe, clean, secure temperature compliant facility with documentation and records to demonstrate compliance to your specific product requirements. Never underestimate and carefully plan customs clearance and use 3PL/logistics partners that have the expertise and trained staff to manage your full supply chain successfully and will inform you immediately (as per signed agreements) of any unplanned events with your products.

**Poor Practice**

The pallet below arrived as one pallet of a 5-pallet delivery. As you can see it is extremely dirty (the shrink wrap should only show pristine white boxes as it is clear shrink wrap). A footprint is evident on the top of the pallet where the integrity is broken.

These 5 pallets arrived from a manufacturer to a large wholesaler, who could not believe a delivery could arrive in such condition. After investigation, they discovered that the pallets were in a temporary storage location for almost two weeks (over Christmas and New Year) in an unapproved facility, with no licence, no security, no temperature control etc.

The pallets were all rejected.



### 9.3.1 & 9.3.3

#### **Good Practice**

The required shipping container should be chosen based on the product; storage/transportation conditions, quantity to be shipped and route of shipping. For example, a small quantity of high value cold chain product to be shipped to Jersey would be best placed in either an active temperature controlled container, or a validated insulated shipper. Whereas, a 26-pallet shipment of +15°C to +25°C product being shipped from a manufacturing plant in India to the UK, would be best shipped in a temperature controlled reefer.

In all cases, the container being used should be checked before loading for any signs of damage which might affect the temperature control of a vehicle or reefer. The container should also be inspected for any signs of debris or potential contaminants left by previous shipments such as chemicals.

Labelling of a shipment should be clear and visible. The use of diagrams such as a picture of a thermometer (example below) is useful, particularly when shipping cross-border.

The IATA label is recommended for time and temperature sensitive products (see link below for more information).

<http://www.iata.org/whatwedo/cargo/pharma/Pages/ttlabel-faq.aspx>

#### **Poor Practice**

Product shipped with no specified temperature requirements or labelling (all 15-25°C products) in vehicles with curtains that cannot ensure temperature compliance and are not secure or safe/acceptable practice.

No consideration of the length of journey or the number of drops and product sensitivity on European journeys.

### 9.3.2

Consideration should be given for the storage and transportation of medicinal products

Shipment method (Air/Ocean/Road).

Size/value/weight of product.

Label requirements: Temperature specified on product labelling.

Route and time requirements (how quickly does product need to be delivered)?

Routes: for example UK to Italy – is the delivery to 1 location, so only 1 drop? Or to 5 possible delivery locations, so 5 drops? There is a totally different risk for the product quality from one delivery point to 5 delivery points. Specific risk assessment must be included in the temperature qualification for the full delivery process mindful of many other variables including seasonality.

Temperature control method (e.g. Dry ice/cool packs, will dry ice need to be replenished during transit?).

Reusable or single use options.

If validation packages are available from the packaging supplier (assessing their suitability for your requirement). Considering solutions that might suit more than one destination and product type/size to reduce solution requirements/costs.

If time & resource permitting - Shipping studies/Route Qualification (OQ/PQ) exercises in advance of solution selection taking into account seasonal extremes at shipping and receiving locations can be very useful.

Sending multiple dummy shipments via required shipment lane with loggers attached to outside of packaging/vehicle/container to build a performance database of:

- Temperature results (internal vs. external where possible)
- Transit times (Identify possible risk areas/delays, including temporary locations)
- 3PL/Freight Forwarder
- Notable events/failures/trends during transit

#### **Good Practice:**

Documented justification for the selection of the packaging system and evidence exists that it will perform under the known environmental conditions.

#### **Poor Practice:**

Having a solution in place without being able to demonstrate suitability of use.

Using a solution outside of its intended use (validation scope).

Reusing damaged packaging or solutions intended for single use only.

#### 9.4.1 & 9.4.2

##### **Good Practice**

Ensure all staff including contractors handling and managing these products are carefully vetted, specially trained and understand their duties and responsibilities meeting national and international legislation to ensure safe and secure handling using well proven procedures and processes that work on a day to day basis. Records and documentation are essential and access controls, alarms and CCTV monitoring should be used where possible to minimise risk. Bona fides of all suppliers, customers (including collection and delivery addresses) and supply chain partners must be established and re-verified on a regular basis and any non-conformances managed in a timely fashion.

24/7 up to date contacts for at least three individuals, with mobile numbers included, as time is critical if an issue arises, especially over a weekend/out of hours.

##### **Poor Practice**

An untrained driver delivered one of these products to the incorrect location on a hospital grounds on a Friday. The POD was unreadable. Fortunately when the pre-12 o'clock delivery did not arrive as normal for dispensing in the afternoon, the supplier was contacted immediately. Happily they successfully delivered a replacement product that afternoon so the patient was fine. The fact that the driver had delivered to the incorrect delivery point is now subject to a full investigation. Unfortunately you don't always get a second chance to deliver to ensure patient safety.

#### 9.4.3

##### **Good Practice:**

Having the required detail to prove solution suitability.

Documented results of Qualification/Validation studies carried out.

Carrying out on-going assessment of solution suitability.

##### **Poor Practice:**

Using a solution with an unsuitable validation package or having had no validation or qualification work carried out (either a legacy product or newly chosen solution).

Using uncontrolled and/or curtain sided vehicles for movement of temperature sensitive product.

Without temperature control, the risk to product is greatly increased.

#### 9.4.4

##### **Good Practice:**

- Ensuring a risk assessment is in place documenting the mapping process and providing justification for the procedures implemented e.g. intervals between mappings
- Implementing a calibration schedule to avoid the calibration status of devices expiring

- Ensuring devices are calibrated at correct range for required environment/s
- Ensuring calibration is traceable to National or International standard and the certificates produced are suitable.
- Documenting any corrective actions or retests for vehicles that fail the mapping test(s)
- Accuracy of recording & control equipment is vital in order to maintain the required temperature but also to be able to prove accuracy, especially in the event of failures & deviations.
- If excursions are extreme enough to result in potential product loss the monitoring equipment will be key to the decision making process as well as possible insurance claims and therefore its accuracy is vital.

Calibration preferably ‘multi point’ and to include vehicle CMPs as well as control probes providing the read out. To achieve multipoint calibrations, probes will need to have flexibility in their length in order to be placed into a dry block calibrator. The probe can then be exposed to conditions across the chosen range and calibrated in situ. If no probe length is available then a reference device can be placed directly next to the probe but this will only provide the option of a single point calibration. Multi point calibration demonstrates accuracy across the range of the environment and should allow for equipment failures or events that will generate unforeseen temps. For example if a fridge normally operates at +5°C but a fault or major event results in temperatures below freezing, the probe calibration points need to ‘bracket’ the target temperature in order to offer documented accuracy at that range e.g. -5°C /+5°C /+15°C.

#### **Poor Practice:**

- Continuing to rely upon devices with a calibration status that has expired (e.g. >12 months)
- Using devices outside of the checked range. E.g. using a device calibrated at 0°C/+5°C /+10°C but in +20°C conditions
- Utilising vehicles that have not been mapped or properly qualified for intended use

#### **Mapping**

Vehicle to be placed ‘outside’ during mapping (large climatic chambers can be used but only generate artificial rather than real life conditions)

Consideration should be given to representative load size, footprint & configurations during the mapping (dummy loads to simulate FULL and HALF LOAD). EMPTY conditions can also be considered to monitor chiller/control performance.

If the vehicle has dual compartment/temperature capability, consideration should be given to mapping in all configuration options that will be used.

Logger placement rational for the mapping should allow for sufficient coverage of the vehicle, covering all top & bottom corners as well as central locations. When using dummy loads, loggers can be attached directly to the load following a similar pattern.

- ‘Bottom’ locations should be at pallet height (15 to 20cm) and ‘Top’ positions should be at the highest point that the product will be placed.

- Vehicle should be fitted with load limit lines within the vehicle to avoid product being stacked too high, compromising air flow. 'Top' positions should not be higher than the load limit line.

If additional power supply option (electrical supply) is fitted (used for ferry crossings and overnight stops) this should be considered during the mapping term (as well as running on engine power).

Consider air outlet temps (place probes to monitor air outlets and inlets).

Place loggers on the outside of the vehicle to document external temps; compare data to look for any trends to internal/external data.

Note the locations of the CMPs (Continuous Monitoring Probe) within the vehicle and make a comparison of the vehicle readings to the mapping data (take into account that the CMPs are often placed above the load limit line and are not at product level).

Consider basic impact tests such as:

- Power-down tests to document time period that the chamber maintains temperature in event of power supply failure
- Door open tests to document process of loading/unloading
  - Record dates and times of start/finish of impact tests and compare to mapping data to assess impact on environment
- If using non-controlled vehicles for temperate product, mapping should still be a consideration and part of a documented risk assessment

A comprehensive mapping with impact tests and representative loads provides documented proof of how the vehicle operates when challenged in the chosen configurations.

It is recommended that this is supplemented by an on-going monitoring programme to capture situations of failure in the supply chain such as traffic delays & mechanical failures - this data will be valuable in proving product condition good or bad. The Vehicle mapping data can be used in order to place the loggers in the highest risk areas.

#### 9.4.5

##### **Good Practice:**

Implementing a monitoring programme based upon a basic risk assessment to justify the quantity and position of data loggers for the shipment (e.g. Mapping data will provide detail of the areas providing the highest risk).

Capturing enough data during shipments to be able to provide sufficient proof of transit if requested. E.g. a study of TAT has been performed looking at the 'Worst case scenario' and this is repeated when the supply routing is changed.

##### **Poor Practice:**

Relying solely on vehicle prints for product acceptance/proof of transit condition.

Having no or insufficient monitoring in place.

#### 9.4.6

##### **Good Practice**

Following validation studies, approved packaging specifications should be defined which cover the expected external temperature conditions for the journey. An SOP should be in place defining:

The type of insulated box to be used (taking into account the expected journey time and amount of product being shipped).

The packaging specification to be used (taking into account the expected journey time and expected external temperatures).

The use of the cool packs:

What temperature should they be acclimatised at?

How long should they be acclimatised for?

A process for identifying how long they have been acclimatised for (stock rotation).

Where they should be placed inside the insulated box.

Any precautions to prevent the cool packs coming into direct contact with product (e.g. insulation, void filler, bubble-wrap).

The reuse of components:

Checks for damage.

Reacclimatising cool packs.

##### **Poor Practice**

Examples:

Not validating the packaging specifications at expected external conditions and journey times.

Not preventing the cool packs from coming into direct contact with the product.

Not packing the insulated boxes in accordance with a validated packing specification.

No processes for ensuring the ice packs are acclimatised at the correct temperature for the required amount of time.

Reusing damaged components.

Not training relevant personnel.

#### 9.4.7

##### **Good Practice**

A defined and documented process (SOP) should be in place for stock rotation of cool packs. There are many ways to do this depending on how long the cool packs need to be acclimatised for, but some examples are:

Have 5 shelves in the freezer and label each one with days of the week Monday – Friday. Use the Ice-packs from the current day and then re-fill the shelf at the end of the day (or first thing the following day).

Have 2 zones in the freezer, load in zone 1 and then transfer to zone 2 after XX hours (depending on validation), only use zone 2 cool packs to pack insulated containers.

When cool packs are loaded into the freezer, use a date stamp to mark the date of entry. Cool packs can only be used XX number of days after the stamped entry date.

Also, the use of an infrared temperature gun to check the temperature of cool packs before use can minimise the risk of incorrectly frozen cool packs being used.

#### **Poor Practice**

Having no defined process in place is likely to result in some or all of the below examples occurring:

Cool packs are placed randomly in the freezer.

Personnel are not sure when the cool packs were loaded.

Personnel are not sure which cool packs should be used.

Cool packs are loaded into and taken from freezers by different shifts, so personnel using the cool packs didn't necessarily load them, meaning that they don't know which ones to use.

Remember, cool packs are usually identical so it is impossible to tell a partly frozen and fully frozen cool pack apart.

#### **9.4.8**

#### **Good Practice**

The most appropriate shipping solution has been determined from knowledge of the supply chain as defined in a procedure based on guidance in 9.4.3.

An SOP should be in place to define the controls required to deliver sensitive medicine e.g.

- i) Type of packaging system for winter/summer conditions for each destination zone.
- ii) Description of the whole supply chain
- iii) Responsibilities e.g. for monitoring data loggers on receipt & approving data logger results; monitoring storage conditions are consistent with the packaging system used etc.
- iv) The expert to be contacted in the event of excursions outside predetermined tolerances, etc.

Capture all of these variables, and someone (as defined in the SOP) should have responsibility for deciding when summer/winter starts and ends. They should also consider hot or cold spells outside of expected seasonal conditions and react accordingly, giving instruction to change the current shipping method.

#### **Poor practice**

Not paying any attention to the seasonal variations will increase the risk of product being exposed to unacceptable temperature conditions during transportation. If no temperature studies are carried out on worst case routes (e.g. China has a very wide range of climates; Norway in January/February or Greece in summer), the product temperatures are unknown and could adversely affect the quality and efficacy of the products.



## Useful links

MHRA review of GDP deficiencies in 2011: <http://www.mhra.gov.uk/home/groups/is-insp/documents/websiteresources/con149838.pdf>