
BRIEFING

〈 1083.2 〉 **Environmental Conditions Management.** USP is proposing a new series of Good Distribution Practices (GDP) general chapters, which were developed as a result of reviewing two existing general chapters, [Good Storage and Distribution Practices for Drug Products](#) 〈 1079 〉 and [Good Distribution Practices for Bulk Pharmaceutical Excipients](#) 〈 1197 〉, and the previously proposed [Good Distribution Practices—Supply Chain Integrity](#) 〈 1083 〉 that appeared in *PF* 38(2) [Mar.–Apr. 2012] but was subsequently canceled. These three general chapters provide information related to the storage, shipment, distribution, and transportation of pharmaceutical components and products. The review showed overlapping and complementary items among these general chapters and highlighted the need to revisit *USP* chapters on GDP from an overarching perspective. The new general chapters will cover material flow beginning with initial procurement and continuing throughout the supply chain to delivery of pharmaceutical components and products, medical devices, and dietary supplements to the end user. The chapters will address four main GDP topics—[Quality Management System](#) 〈 1083.1 〉, [Environmental Conditions Management](#) 〈 1083.2 〉, [Good Importation and Exportation Practices](#) 〈 1083.3 〉, and [Supply Chain Integrity and Security](#) 〈 1083.4 〉—each highlighting best practices and principles.

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Add the following:

〈 1083.2 〉 ENVIRONMENTAL CONDITIONS MANAGEMENT

INTRODUCTION

Environmental Conditions Management is a system put in place to control environmental conditions (e.g., temperature, relative humidity, light, oxygen, shock, vibration, and other conditions) that can affect the quality of materials and products in the supply chain.

During storage and distribution, the following two approaches can be used to keep the product within its required labeled specifications:

- Controlling the environmental conditions in equipment, storage rooms, and transportation vehicles, where applicable, by means of devices such as a heating, ventilation, and air-conditioning (HVAC) system, refrigerator, or (de)humidifier

- Using packaging materials that allow the control of environmental conditions (e.g., insulated containers, thermal blankets, temperature stabilizers, desiccants, light-resistant material)

Whichever approach is used, the system should be qualified or monitored for validation or both.

The scope of this chapter provides general guidance on key aspects of the control of environmental conditions during the distribution of products. It is not intended that this chapter establish temperature ranges and relative humidity control or other environmental conditions to maintain the integrity of the material or product during distribution. (See [Packaging and Storage Requirements](#) < 659 > for temperature-related definitions.)

The chapter is structured in five sections as shown in [Figure 1](#).

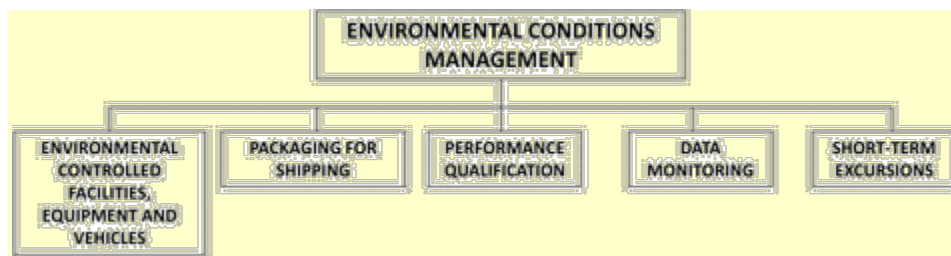


Figure 1. Environmental conditions management—chapter structure.

ENVIRONMENTAL CONTROLLED FACILITIES, EQUIPMENT, AND VEHICLES

General requirements for storage facilities, equipment, and dedicated transportation vehicles are provided in [Quality Management System](#) < 1083.1 > , [Resources Management](#). In this chapter, facilities, equipment, and transportation vehicles are emphasized as systems functioning to control environmental conditions in accordance with product specifications.

The organization should have a written procedure for the storage and transportation of materials or products, taking into account the following as appropriate:

- Material or product category (narcotics, medical devices, prescription pharmaceuticals, temperature sensitive, hazardous products, and others)
- Layout (e.g., floor-standing pallets, pallet racking, boxes inside the refrigerators, and others)
- Volume of stored product (including peaks of storage)
- Air circulation and environmental conditions (e.g., temperature, relative humidity, pressure, and other conditions)
- Contingency plan for outages and breakdowns

The procedure should be written on the basis of a risk assessment of factors that can impact material or product quality during storage.

All facilities, equipment, and dedicated temperature-controlled transportation vehicles should be challenged under a performance qualification protocol.

PACKAGING FOR SHIPPING

The organization should have a written procedure for the passive packaging system used for shipping. The procedure should be written on the basis of an assessment of risk factors that can impact material or product quality during shipping, including but not limited to the following:

- Protection required for the material or product
- Environmental conditions (e.g., temperature and relative humidity) at which the material or product can be transported and temporarily stored (e.g., receiving, shipping, customs areas)
- Packaging system selection and auxiliary packaging materials used for shipping, with selection based on the specified storage conditions for the material or product and the transportation mode, lanes, and duration
- Package configuration for shipping, based on qualification studies (e.g., how many gel pack layers, location of gel packs, and other factors)
- Monitoring device requirements: quantity, type, and position within the package system (see [Monitoring Devices—Time, Temperature, and Humidity < 1118 >](#))
- Tamper-evident closure systems for the packaging system
- Forms or records or both to register data during shipping and temporary storage
- Documentation necessary for shipping (e.g., labeling, tamper-evident seals, courier documents, and others)

Labeling should provide all the information necessary to comply with national and international guidelines on GDPs, environmental conditions during distribution, and compliance with any other national or international rules and regulations.

PERFORMANCE QUALIFICATION

Performance Qualification (PQ) should be carried out to evaluate if the equipment, warehouse facilities, utilities, shipping containers, and dedicated temperature-controlled vehicles perform as required.

Performance qualification can be any of the following:

- **Prospective:** When documented evidence for PQ is generated before the start-up of the operation or system (e.g., using laboratory simulations for shipping containers or transportation modes)
- **Concurrent:** When documented evidence for PQ is generated during the actual operation of the system (e.g., real-time monitoring of an actual shipping container or storage area)
- **Retrospective:** When documented evidence for PQ is generated using historical data for systems (e.g., temperature/humidity monitoring logs)

PQ for transport systems (shipping container and dedicated vehicles) should reflect actual load configurations and expected environmental conditions.

Testing should be performed on both active and passive thermal packaging systems. Organizations should perform a prospective PQ (simulating the distribution environment to perform challenge tests) when appropriate, and then a concurrent qualification when products are monitored in their shipping environment.

For organizations that are shipping products without a prospective or concurrent PQ, each cargo should be monitored and a retrospective PQ done using historical data and a risk assessment to justify the method used.

Spot checks using calibrated monitoring systems should be done periodically to ensure maintenance of the shipping qualification status (for transportation methods not using monitoring for each shipment) and to support risk assessment.

For shipping container PQ, several standards are available for evaluating performance of packaging systems during transportation. Organizations with standard test methods for this purpose include the American Society for Testing and Materials (ASTM) and the International Safe Transit Association (ISTA).

PQ protocols should be approved prior to execution. Thermal PQ protocols should be written to ensure that shipping containers, dedicated vehicles, and storage facilities can maintain the temperature range specified for the product, even when faced with extreme outside temperatures. The protocol should take into account, where applicable, at least the following:

- Responsibilities, including third parties
- Material or product storage requirements as established by means of stability studies (temperature and relative humidity ranges allowed during storage and transportation)
- Description of the storage room or payload compartment, including dimensions, layouts, active environmental controls (coolers, heaters, mechanical stabilizers for minimizing vibration, and others), temperature stabilizers, and power systems (electrical, battery, and others)
- Location and volume of the material or product inside the storage room or shipping container
- Packaging material
- Environmental conditions during storage and transportation
- Transportation mode, route, and duration
- Monitoring devices and alarms (warning systems) in place
- Frequency of data logging
- Location and number of monitoring devices for temperature and humidity (where applicable)
- Temperature mapping to show whether temperatures are evenly distributed or if there are hot or cold spots in storage areas and dedicated vehicles
- Acceptance criteria and approvals
- Audible or visible alarms or both should be in place if temperature or relative humidity or both are out of specification. These alarms should be qualified and also periodically challenged.

DATA MONITORING

All storage facilities and dedicated vehicles should be monitored for environmental conditions.

All monitoring devices should be calibrated according to their intended use, and at least annually. For more information, see chapter [〈 1118 〉](#). The organization should have written SOPs for the operation of the device, calibration frequency, monitoring interval, data recording, data interpretation (including alarms), and contact information for responsible personnel who will assess any excursions during storage, transport, or upon receipt.

Data loggers or sensors placed inside shipping containers for temperature, relative humidity, or shock and vibration monitoring should be checked and data downloaded (where applicable) upon receipt of the cargo. Environmental Condition & Delivery Time charts (e.g., temperature vs. time or relative humidity vs. time) are useful tools to check the environmental exposure profile of the cargo during the shipping, transport, and delivery to the customer, and to allow the evaluation of any excursions.

SHORT-TERM EXCURSIONS

Short-term excursions can occur during distribution. Any excursion should be documented and handled as a nonconformance or deviation report. Product disposition should be established on the basis of an assessment of the excursion (e.g., the temperature or relative humidity to which the material or product was exposed, and for how long), the stability data obtained from traditional stability studies (under accelerated and long-term conditions and performed in accordance with International Conference on Harmonisation (ICH) guidelines), and distribution stability studies (e.g., extremes of temperature, temperature-cycling, and freeze-thaw studies, as appropriate). Combining stability data from long-term and accelerated studies, mean kinetic temperature calculations, temperature excursion studies, and temperature cycling studies should provide the information necessary to evaluate the effect of excursions on material or drug product quality that may occur during the storage and transportation process.

Systematic excursions, however, should be handled as corrective and preventive actions (CAPAs) (see [〈 1083.1 〉](#)).

APPENDIX

In the context of this chapter, the following definitions are used.

Active packaging container: Actively powered systems that use electricity or other energy to maintain a specific temperature range inside an insulated container or enclosure.

Auxiliary packaging material: Loose packaging material (e.g., strong cardboard, dunnage, pieces of polystyrene, air bags, bubble wrap) used to protect the material or product from damage during transport.

Distribution hazards: All environmental factors to which a material or product can be exposed during distribution, such as vibration, pressure, stacking load, temperature,

and relative humidity.

Mean kinetic temperature (MKT): The single calculated temperature at which the total amount of degradation over a particular period is equal to the sum of the individual degradations that would occur at various temperatures. It is not a simple arithmetic mean. MKT may be considered as an isothermal storage temperature that simulates the nonisothermal effects of storage temperature variation.

Passive packaging container: Systems that maintain a controlled environment inside an insulated container or enclosure without an external source of energy.

Performance qualification (PQ): The documented verification that facilities, systems, and equipment, as installed, operate robustly and reproducibly within the specification established by the organization. For the purpose of this chapter, performance qualification means all tests designed and executed to determine if the storage rooms and areas, equipment, dedicated temperature-controlled transport vehicles, and shipping containers are suitable for their intended use.

Temperature stabilizer: A material or combination of materials that stores and releases thermal energy in an effort to maintain a specified temperature range within an active or passive packaging system (e.g., water-, chemical-, or oil-based phase change material, such as carbon dioxide, solid/dry ice, and liquid nitrogen).