Technical Report No. 39 Cold Chain Guidance for Medicinal Products: Maintaining the Quality of Temperature-Sensitive Medicinal Products Through the Transportation Environment

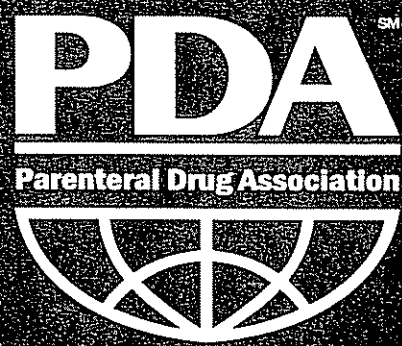
PDA Journal of Pharmaceutical Science and Technology

September/October 2005

Supplement

Volume 59

No. S-3



PDA Technical Report No. 39

Cold Chain Guidance for Medicinal Products: Maintaining the Quality of Temperature-Sensitive Medicinal Products Through the Transportation Environment

PDA Cold Chain Management Task Force

Rafik H. Bishara, Ph.D., Eli Lilly and Company—ret. (Chair and contact person)

Jim Antonopoulos, sanofi pasteur

Mari Bakken, Abbott Laboratories

Daniel Colton, Genentech Inc.

Laura Fontan, Human Genome Sciences

Derrick Gallagher, Sanofi-Aventis

Paul Harber, Eli Lilly and Company

Kelly Klien, Wyeth

Chris Landauer, Eli Lilly and Compnay

Teresa Lucas, Eli Lilly and Company

Sarvang Mishra, Wyeth

Kevin O'Donnell, Abbott Laboratories

Oumer Salim, Wyeth

Jeff Seeley, Merck & Co., Inc.

Bob Seevers, Ph.D., Eli Lilly and Company

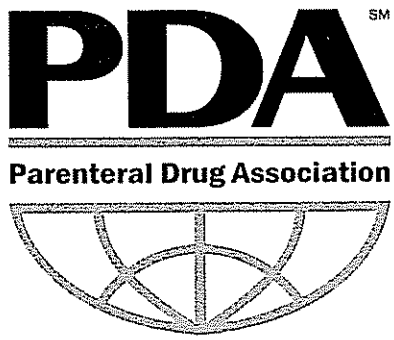
Edward G. Smith, Ph.D., Wyeth

Douglas Staruk, Wyeth

Donald Wilson, Amgen Inc.

Cold Chain Guidance for Medicinal Products

Technical Report No. 39
Supplement
Vol. 59, No. S-3
September/October 2005



TECHNICAL REPORT # 39: COLD CHAIN GUIDANCE FOR MEDICINAL PRODUCTS: MAINTAINING THE QUALITY OF TEMPERATURE-SENSITIVE MEDICINAL PRODUCTS THROUGH THE TRANSPORTATION ENVIRONMENT

Table of Contents

This document should be considered as a guide; it is not intended to establish any mandatory or implied standard.

I. Introduction

Medicinal products requiring controlled temperature storage should be transported by appropriately specialized means to ensure product quality is not adversely affected during transport. These products may be shipped outside of their respective label storage conditions provided stability data exist demonstrating that product quality is not affected.

This document presents a design approach to develop specialized packages and systems that will protect temperature-sensitive products during transport. The design approach is comprised of three elements. These elements are (1) Identification of Requirements, (2) Development, and (3) Implementation.

The distribution environment can vary greatly, especially when transporting medicinal products between climatic zones. Seasonal changes, mode of transportation, and regional regulations and capabilities are also variables that must be considered within the transportation environment. These variables should be evaluated on a case-by-case basis.

Global regulatory expectations and compendial standards regarding good storage and shipping practices and time, temperature, and humidity monitoring devices have been put forth by WHO, EU, Canada, and USP.

Purpose

The purpose of this document is to provide guidance to industry on the essential principles and practices of transporting temperature-sensitive medicinal products through the transportation environment. This process is commonly referred to as "cold chain." This guidance has necessarily been written at a high level. As befits a guidance document, it enunciates the *what* without providing prescriptive detail on the *how*.

Scope

The process defined in this document is for thermally controlled transportation of medicinal products. The same principles may also be applicable for intermediates, active pharmaceutical ingredients (APIs), and diagnostic products that require thermally controlled transportation.

The level of guidance provided herein should allow firms to develop their own processes and also be aligned with CDER's General Principles of Process Validation as adapted in this guidance:

- Component Qualification (CQ)
    - Establishing confidence that ancillary components are capable of consistently operating within established limits and tolerances
- Operating Qualification (OQ)
    - Establishing confidence that the process is effective and reproducible
- Performance Qualification (PQ)
    - Establishing confidence through appropriate testing that the product produced by a specified process meets all release requirements for functionality

The above principles may be used to reliably qualify the cold chain distribution process. Even a qualified process is subject to change over time. Therefore, periodic and appropriate monitoring is recommended. The frequency and type of monitoring will be based on the specific conditions of a given distribution process.

The diagram in Figure 1 shows an overview of the medicinal cold chain management process flow.

II. Principles of Qualification for Transport

The principles of qualification for the transport of temperature-sensitive medicinal products closely follow established guidelines and regulations for qualifying the manufacture of these same products. These include

- Development of specifications, processes, systems, and components
- Written procedures
- Approved protocols and reports
- Justified test methods and acceptance criteria
- Qualification testing that challenges "anticipated extremes"

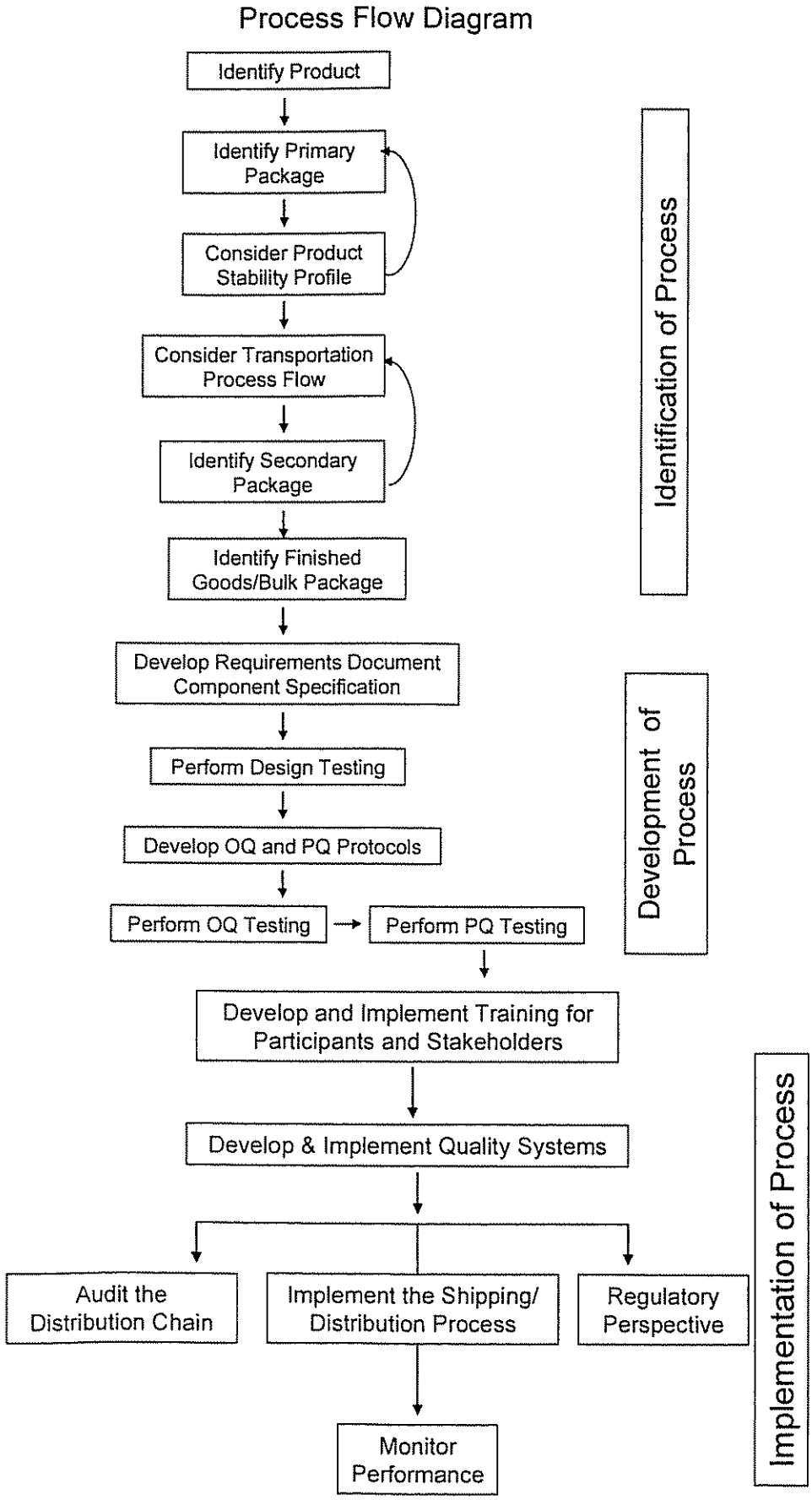

Process Flow Diagram
Identify Product
Identify Primary Package
Consider Product Stability Profile
Consider Transportation Process Flow
Identify Secondary Package
Identify Finished Goods/Bulk Package
Develop Requirements Document Component Specification
Perform Design Testing
Develop OQ and PQ Protocols
Perform OQ Testing
Perform PQ Testing
Develop and Implement Training for Participants and Stakeholders
Develop & Implement Quality Systems
Audit the Distribution Chain
Implement the Shipping/ Distribution Process
Regulatory Perspective
Monitor Performance
Identification of Process
Development of Process
Implementation of Process

Figure 1

- Ongoing monitoring or periodic evaluation
- Change control

Medicinal products are transported in a commercial environment as opposed to a controlled laboratory environment. Therefore, factors such as unforeseen transport events and the weather affect the actual conditions a specific shipment may encounter. These factors should be considered when designing test protocols and in understanding "anticipated extreme" challenges.

III. Product Stability Profile

Medicinal products must be transported in a manner that ensures products will be maintained within an acceptable temperature range. This range may differ from the conditions specified for long-term storage and is determined by performing product temperature-excursion studies. The objective of this section is to outline studies for evaluating the impact of temperature excursions on product stability that may occur during transport of medicinal products.

Figure 2 shows the basic principles of the proposed studies.

These studies will expose medicinal products to temperature conditions both within and outside of long-term storage conditions.

1. Long-term stability study—ICH Q1A
2. Accelerated stability study—ICH Q1A
3. Temperature excursion study—FDA 1998 Draft Stability Guidance (see Appendix, Tables I to IV).

The idea is to evaluate stability data from long-term and accelerated stability studies, temperature-excursion studies, and/or thermal cycling studies to predict the impact of temperature excursions on medicinal product quality during the transportation process. An example of a comprehensive study design for a refrigerated product to generate sufficient stability data to determine the potential effect of temperature excursion on product quality is presented in Table V. In this example, the product has three strengths; in addition to long-term and accelerated stability data, a bracketing approach is used in which the high and low strengths are also tested under freezing conditions, at 40°C, and under temperature cycling conditions. Other study designs may be used as appropriate.

Table VI is an example of compiling the results of the stability studies from the example protocol shown in Table V. This then would serve as a guide to the type and extent of temperature excursions that would be supported by the stability data for this example product. Transportation stability study results from Table V have been used to write the Transportation Control Strategy document shown in Table VI. The stability data support the temperature excursions for the time periods indicated. Note: a table such as Table VI must be constructed for each product based on product-specific stability data.

The process described covers newer products for which ICH stability data are available. Pre-ICH Guidance products will need to be assessed on a case-by-case basis.

Principle	Reference
Long-term and accelerated stability studies are run on final formulation in final primary package	ICH Q1A
Transportation studies designed to include anticipated ambient temperature variation and duration are run when primary stability studies are initiated	Company Decision
Upon completion of transportation study, samples may be placed on long-term-stability testing conditions	Company Decision

Figure 2

Proposed Stability Studies

A Note on Storage Temperature vs. Distribution Temperature: Storage temperatures of drug products are relatively constant, and stability studies intended to support storage conditions take into account expected variations of storage temperatures; thus drug products intended for storage at 20°C are tested at 25°C. It is not possible to control the temperature of product in the same way during the distribution process; therefore additional studies at extreme temperatures (e.g., elevated or freezing temperatures) must be performed. Long-term storage or label storage temperatures may be different from short-term shipping/distribution temperatures.

IV. Transportation Process Flow Considerations

Development of Temperature Profiles for Use in Qualification Studies

In order to perform qualification studies of controlled temperature shipping packages and systems, it is typically necessary to conduct laboratory testing to thermally challenge the packages and systems. These tests should be conducted using environmental temperature profiles that are typical of the conditions that the package will encounter during a shipment. In order to develop the testing profiles, the shipper should consider a number of factors, including but not limited to

- Temperature conditions at origin and destination points
- Seasonal temperatures (winter vs. summer)
- Transport routes and modes (overnight air, ground, international, etc.)
- Total duration of transit
- Duration and location of various handling/stopover points along routes
- Product handling and logistics at various handling/stopover points along routes

Whenever possible, environmental profiles should be based on realistic expectations of transport temperatures, which are developed using scientifically sound criteria. This may be done using field-testing (monitoring) of actual shipments, review of historical environmental data, review of published standards (i.e., ISTA 7D), or by other means. Profiles should include anticipated extreme conditions in order to challenge the effectiveness of the cold chain package or system, whenever possible.

Anticipated extremes in ambient temperatures to which the product may be exposed are sometimes referred to as "summer" and "winter" or "hot" and "cold" temperature profiles. Where actual historical temperature data in transportation is not available, the scenarios may be defined by calendar months or actual temperatures at product origin, product destination, along the transport route, and at transportation hubs (as applicable). Sound rationale should be provided for the process used in developing temperature profiles used in transport qualification testing.

Packaging

A container/closure system can be comprised of one or multiple packaging components. The container closure system refers to the sum of the packaging components that together contain and protect the dosage form or drug product.

Container/closure system components are divided into two types: primary and secondary. A primary packaging component is one that is or may be in direct contact with the dosage form. Some examples of primary components are vials, syringes, bottles, rubber closures, and container or closure liners. A secondary component is one that is not, nor will be, in direct contact with the dosage form. Some secondary packaging components are stopper overseals, overwraps, cartons, and container labels.

A market package includes the container closure system, any associated components (e.g., dosing cups, droppers), and external packaging (e.g., cartons, shrink wrap). The market package is the unit provided to a pharmacist, hospital, or retail customer upon purchase but does not include packaging used solely for transportation (e.g., corrugated boxes or insulated containers).

Shipment under cold chain controls may be required for both market packages and any precursors to the market package such as APIs, intermediates, excipients, bulk-packaged drug products, or packages of multiple units of the labeled or unlabeled drug product in its container closure system (e.g., vial or syringes). It is important to identify the container closure system because it is the entity that must be temperature-controlled during the transport process. Packaging must be identified to determine the amount of thermal mass that must be temperature-controlled. The greater the thermal mass, the less reactive it is to ambient temperature variation.

The purpose of secondary packaging is to identify, protect, market, and communicate information about the product. Examples of secondary packaging include labels, cartons, and trays. The materials and components

selected for the secondary package may affect the design of the transportation container and/or system.

Secondary packaging must be identified to determine the minimum and maximum product loads that can be placed within the transportation container. Secondary packaging also determines the number of primary packages that can be placed within it. The more empty space within the secondary package not utilized by the thermal mass of the product, the more difficult it is to control the system thermally.

V. Design and Development

Functional Requirements Document

The functional requirements document is the summary of the Identification of Requirements process step. The purpose of this step is to document the critical parameters of the product, packaging, and transport system previously identified in Sections I through IV. Critical parameters include

- Transportation (e.g., duration, mode(s), route(s))
- Product stability (e.g., temperature range established)
- Packaging (e.g., bulk or finished goods)

Component Specification (CS)

This section of the guidance outlines general principles that apply to product impact components for the transport process. Product impact components are those that may reasonably be expected to have a direct effect on the performance of a transportation system. Examples of product impact components include insulated containers and refrigerants. The component specification establishes confidence that components are capable of consistently performing within established limits and tolerances.

A specification should be generated to outline component requirements as applicable. This specification may include, but is not limited to

- Material requirements
- Mechanical requirements
- Dimensional requirements
- Printing requirements
- Storage requirements
- Sampling requirements
- Weight requirements
- Calibration limits
- Fragility limits
- Shock and vibration limits
- Insulation requirements

Design Testing

Design testing should be performed prior to qualification testing. Design testing is performed to ensure that functional requirements are met by the proposed package or system. Design testing process parameters typically include, but are not limited to

- Process duration
- Quantity, temperature conditioning, and location of refrigerant
- Type of insulating material
- Minimum and maximum thermal mass

The outcome of design testing assures a high confidence for successful operational qualification (OQ) of a specific package or system. The results of design testing should be formally documented in a report. Design testing is illustrated in Figure 3.

VI. Qualification Testing: Operational Qualification (OQ) and Performance Qualification (PQ)

A Note on Qualification vs. Validation: Qualification is documented testing that demonstrates with a high degree of assurance that a specific process will meet its predetermined acceptance criteria. Validation is documented testing, performed under highly controlled conditions, that demonstrates that a process consistently produces a result meeting pre-determined acceptance criteria. Therefore, transportation processes can be qualified rather than validated, since it is not possible to control, in the real world, all the parameters that could affect the transportation process (e.g., weather, customs and traffic delays, mechanical failures, etc.). Even a qualified process is subject to change over time. Therefore, periodic and appropriate monitoring is recommended. The frequency

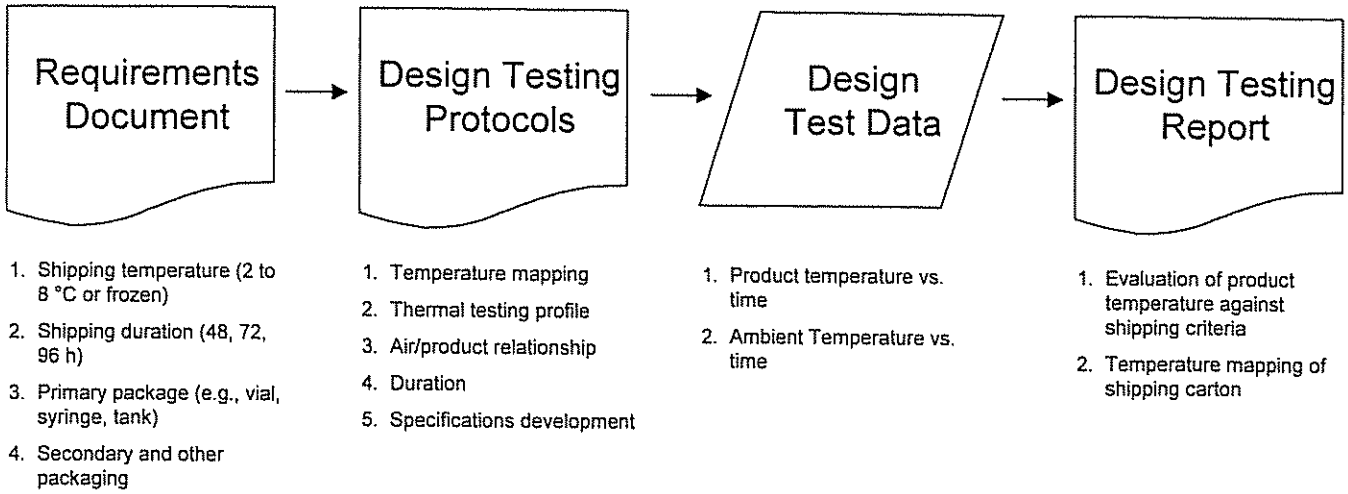


Figure 3

Design Testing Process

and type of monitoring will be based on the specific conditions of a given distribution process.

OQ/PQ must be performed using the designated transport configuration to provide assurance that product quality is maintained during transport. Qualification testing and results should be documented in a formal report.

The OQ and PQ protocols, test plans, or SOPs should contain at a minimum the

- Testing objective
- Scope
- Materials description
- Equipment description and calibration information
- Critical quality attributes
- Critical performance parameters
- Test methods and rationale
- Acceptance criteria

Qualification Protocol

Formal qualification testing should always be performed under a pre-approved protocol, test plan, or SOP. Testing typically consists of OQ and PQ testing.

OQ Testing

Testing may be performed using temperature-controlled environments (i.e., temperature chambers) or actual shipments at ambient temperatures (i.e., field testing), as appropriate, based on the projected transportation channel. The testing should reflect actual transportation load conditions and configurations, and it should capture expected extremes anticipated.

Product or approved representative material may be used in qualification testing. Rationale for using approved representative material should be included in the qualification protocol.

All packaging components used in testing should be approved for use.

Calibrated temperature monitors should be placed directly in contact with the product or representative product, if possible, to collect temperature data. Sufficient positions within the load should be monitored to get representative temperature data on variances that may be inherent to the load packing, load configuration, or manner of transport.

OQ testing should include but is not limited to

- Use of temperature profiles designated according to Section IV
- Duration beyond what is anticipated for the transport process

- Minimum and maximum transportation load configurations
- Defined packing configuration(s)
- Calibrated temperature monitors
- A sufficient number of tests to assure reliable results
- Identification of temperature-monitoring locations for PQ

PQ Testing

PQ testing consists of consecutive, replicate field transportation tests to demonstrate that the process is effective and reproducible.

Testing is performed using typical load configurations. Sound rationale to justify the test methods, number of tests, and load configurations (as applicable) should be stated in the protocol.

PQ testing should include

- Actual ambient temperature variances, including seasonal changes customary in transportation
- Representative transportation load configurations
- Defined packing configuration(s)
- Calibrated temperature monitors
- A sufficient number of tests to assure reliable results

VII. Process Implementation and Training

The specific transport systems and cold chain packaging systems are confirmed during qualification. Transfer of the qualified process to the operational areas is formally accomplished by means of writing approved procedures that will result in repeatable, successful transport of medicinal products. The written approved procedures should be in place and responsible personnel should be trained prior to implementation of the process. Consideration should be given to the attachment of procedures used in the PQ report.

Training should provide instruction to relevant personnel and organizations participating in the cold chain process (i.e., process stakeholders) concerning the principles of packaging, qualifying, and transporting temperature-sensitive medicinal products.

VIII. Quality Systems

Auditing and Process Assessment

Regulated good manufacturing processes and systems used for transportation of temperature-sensitive medicinal products require a foundation of quality systems to support their use. These systems provide a high degree of assurance that the qualified transportation system will continue to perform as intended.

The quality systems should include the following, as applicable:

- Approved written procedures and specifications
- Calibration program
- Stability program
- Qualification program
- Deviation and investigation program
- Corrective and preventive action program (CAPA)
- Training program
- Audit program
- Periodic cold chain process assessment
- Change control program

Regulatory

A distinction is properly made between data that should be included in regulatory submissions, such as ICH stability data to support product expiration dating in its primary container, and data generated solely to support shipping, distribution, and logistics, which may include the following elements. Such data would be retained at the manufacturing site and shared with regulatory inspectors on request.

Discussion of product transportation routes

- Manufacturing/packaging site(s)
- Description of logistics

Discussion of product configuration(s)

- Product being transported
- Product packaging
- Post-transport disposition process

Stability Program Details

- Data to support excursions anticipated during transport

IX. References

International Conference on Harmonization (ICH) Q1A (R2) Stability Testing of New Drug Substances and Products (originally published 1994, revised 2003).

World Health Organization (WHO) Technical Report Series, No. 863, Annex 5 Guidelines for stability testing of pharmaceutical products containing well established drug substances in conventional dosage forms (1996).

United States Food and Drug Administration (FDA) Process Validation Requirements for Drug Products and Active Pharmaceutical Ingredients Subject to Pre-Market Approval (Originally published in 1987, revised 2004).

United States Food and Drug Administration (FDA) Guidance for Industry: Stability Testing of Drug Substances and Drug Products (Draft, 1998).

Guidelines on Good Distribution Practice of Medicinal Products for Human Use, European Union, 1994.

Good Distribution Practices (Gdp) For Pharmaceutical Products, World Health Organization (draft 2004).

Guidelines for Temperature Control of Drug Products during Storage and Transportation—Draft (GUIDE-0069), Health Canada, December 2004.

Thermal Controlled Transport Packaging for Parcel Delivery System Shipment, International Safe Transit Association Test Procedure 7D.

USP General Chapters ⟨1079⟩ Good Distribution Practices, and ⟨1118⟩ Monitoring Devices-Time, Temperature, and Humidity.

X. Glossary

Associated Packaging Components: Components used to deliver a drug product but are only in transient contact with the drug product. (e.g., dosing cups, droppers).

Bulk/Intermediate Product: Consists of solid, liquid, or frozen product in a bulk container configuration such as a bag, tank, or drum. The product may be in these container configurations between process steps or prior to filling into vials, ampoules, cartridges, or syringes.

Cold Chain: The sequence of transportation events, from the manufacture of the formulated bulk material through receipt of the final packaged product by the end-user, that maintains temperature sensitive products within approved temperature specifications. Maintaining temperature control during these transportation events assures that product quality is maintained.

Container Closure System (CCS): The sum of the packaging components that contain and protect the drug product (primary components + secondary components), if the secondary components are intended to provide additional protection to the drug product (e.g., glass vial + rubber closure + aluminum overseal).

Critical Quality Attributes: Attributes that describe a parameter or item that must be controlled within predetermined criteria to ensure that the medicinal product meets its specification (ICH Q7A).

Distribution: Transport of finished product from a drug manufacturer's warehouse/storage facility (i.e., distribution center (DC)) to external commercial customers or clinical facilities. Subsequent distributions may also occur.

Distribution Temperature: The temperature range, supported by stability studies, within which a medicinal product can be transported for a short duration of time without adverse effect on quality parameters.

Finished Product: Consists of solid, semi-solid (e.g. ointment), liquid, or frozen product in its final market package. This typically refers to the product/package that is sent from a manufacturer/packager to a distributor or retail customer. The product may be in a bulk container configuration, such as a tank or drum, or in vials, ampoules, cartridges, or syringes, etc.

Market Package: The final package presentation intended for the end user but not including packaging used

solely for transportation (e.g., bottle + cap liner + screw cap + label + dose cup + carton + SKU; may contain multiple cartons of product).

Medicinal Product: Any product intended for the diagnosis, treatment, or prevention of disease.

Operational Qualification (OQ): Transport tests that are conducted in a temperature-controlled chamber or by other simulated test protocols. Generally, simulated testing is conducted using a temperature profile that contains the anticipated extremes for the transportation duration and temperature.

Performance Qualification (PQ): Transport tests of product or placebo that is conducted during actual transportation or distribution.

Primary Package: The container/closure system that is in or may be in direct contact with the medicinal product (e.g., vials, stoppers, syringes).

Product Impact Components: Those parts of the packaging system that may have the potential for affecting the thermal stability or protection of the medicinal product being transported. Examples of product impact components include insulated containers and refrigerants used in the transport package or system.

Qualification: Documented testing that demonstrates with a high degree of assurance that a specific process will meet its pre-determined acceptance criteria.

Secondary Package: A component that is not nor will not be in direct contact with the drug product. (e.g., vial seals, overwraps, container labels).

Shipping: The transit of any material by land, sea, or air from one site to another. This may include intra-plant movements.

SKU: Stock-keeping unit.

Stability: The capacity of a drug substance or a drug product to remain within specifications established to ensure its identity, strength, quality, and purity throughout the retest period or expiration dating period, as appropriate.

Stability Profile: The physical, chemical, biological, and microbiological behavior of a drug substance or drug product as a function of time when stored under the defined environmental conditions of an approved protocol.

Stability Transportation Study: Study performed to generate data to evaluate the effect of temperature variation during transportation on product quality.

Storage Temperature: The temperature range listed on the medicinal product label specified for long-term storage.

Supply Chain: The process by which a drug product is shipped and distributed from the manufacturer to the end user.

Temperature Excursion: Any event in which product is exposed to temperatures outside of the recommended storage and/or transport temperature range.

Temperature-Sensitive Products: Products whose quality may be adversely affected by temperature extremes (e.g., frozen, refrigerated, and certain controlled room temperature products).

Transportation: Movement of medicinal product within a designated supply chain.

Transport Duration: The time from preparing goods for transport until receipt of goods. This includes, but is not limited to

- Preparation
- Loading
- Transit
- Intermediate storage
- Unloading

Transport Temperature Profile: Anticipated ambient temperature variation and duration to which product may be exposed during transportation. When OQ is conducted in a temperature-controlled chamber, the temperature profile should include a temperature challenge that is higher or lower than the anticipated ambient profile.

Validation: Documented testing, performed under highly controlled conditions, that demonstrates that a process consistently produces a result meeting pre-determined acceptance criteria.

XI. Appendix

Note: the ICH and WHO stability tests are performed on the product in its primary container.

TABLE I
Long-term Stability Study

Storage Condition	Testing Condition ICH Q1A	Testing Condition WHO Annex 5
Controlled Room Temperature 20 to 25°C	25°C/60% RH for 12 months	30°C/65% RH for 12 months
Refrigerated Condition 2 to 8°C	5°C for 12 months	5°C for 12 months
Freezer Condition −20 to −10°C	−20°C for 12 months	−20°C for 12 months

TABLE II
Accelerated Stability Study

Storage Condition	Testing Condition ICH Q1A	Testing Condition WHO Annex 5
Controlled Room Temperature 20 to 25°C	40°C/75% RH for 6 months	40°C/75% RH for 12 months
Refrigerated Condition 2 to 8°C	25°C/60% RH for 6 months	—
Freezer Condition −20 to −10°C	5°C for 6 months	—

TABLE III
Temperature Excursion Study

Storage Condition	Testing Condition ICH Q1A	Testing Condition WHO Annex 5
Controlled Room Temperature 20 to 25°C	1) −20°C for 2 days 2) 60°C/75% RH for 2 days	—
Refrigerated Condition 2 to 8°C	1) −20°C for 2 days 2) 40°C/75% RH for 2 days	—
Freezer Condition −20 to −10°C	1) 25°C/60% RH for 2 days	—

Note: testing conditions in Table III and Table IV may be adjusted according to product-specific needs. Alternative study designs may be used as appropriate.
RH = relative humidity.

TABLE IV
Thermal Cycling Study

Storage Condition	Testing Condition ICH Q1A	Testing Condition WHO Annex 5
Controlled Room Temperature 20 to 25°C	−20°C for 2 days followed by 40°C/75% RH for 2 days Repeat for a total of 3 cycles	—
Refrigerated Condition 2 to 8°C	−20°C for 2 days followed by 25°C/60% RH for 2 days Repeat for a total of 3 cycles	—
Freezer Condition −20 to −10°C	−20°C for 2 days followed by 5°C for 2 days Repeat for a total of 3 cycles	—

RH = relative humidity.

TABLE V
Example of a Comprehensive Study Design for a Refrigerated Product

Product Group	Item Code	Description	Storage Condition	Routine 5°C	Accelerated 25°C/60% RH	Excursions −20°C	Excursions 40°C/75% RH	Excursions Cycling*	Comments
XXXX Vials	VL123	5 mg	Refrigerated	24 months	6 months	2 days	2 days	Cycling*	Transportation Study Technical Report Tryyyy—Excursion TRzzzz—Cycling
XXXX Vials	VL456	10 mg	Refrigerated	24 months	6 months				
XXXX Vials	VL789	20 mg	Refrigerated	24 months	6 months	2 days	2 days	Cycling*	Transportation Study Technical Report Tryyyy—Excursion TRzzzz—Cycling

* −20°C for 2 days followed by 25°C/60% RH for 2 days (repeat for a total of 3 cycles).
RH = relative humidity.

TABLE VI
Example of a Transportation Control Strategy Document Based on Product-Specific Stability Data to Determine the Effect of Temperature Excursions

Storage Condition: Refrigerated Condition (2 to 8°C)

Temperature Range	Time
< −20°C (< −4°F)	Do Not Use
−20 to 2°C (−4 to 36°F)	2 days
2 to 8°C (36 to 46°F)	Until Expiry
8 to 25°C (46 to 77°F)	6 days
25 to 40°C (77 to 104°F)	2 days
>40°C (104°F)	Do Not Use

PDA Journal of Pharmaceutical Science and Technology

PDA Journal of Pharmaceutical Science and Technology (ISSN 1079-7440) is published biomonthly by the PDA, Inc., 3 Bethesda Metro Center, Suite 1500, Bethesda, MD 20814.

Subscriptions—PDA membership dues include an annual subscription to the *PDA Journal of Pharmaceutical Science and Technology*. For an application form and information regarding membership, address the Association. Industrial, university, and public libraries, as well as government agencies, may subscribe at the rate of $270 (U.S.) per year. Back issues are available from the Association at the rate of $55 members/$250 nonmembers plus shipping. Copies of individual articles are available at a cost of $20 members/$215 nonmembers, plus shipping (please specify volume number, issue, and title of article: this information may be referenced at *www.pda.org*).

Claims—Issues lost in transit will not be replaced if claim is received more than 90 days from date of issue or if loss was due to failure to give notice of change of address. The Association cannot accept responsibility for delivery outside the United States when shipment has been made by first-class mail.

Periodicals postage paid at Bethesda, Maryland and additional mailing offices. Postmaster: Send address changes to the *PDA Journal of Pharmaceutical Science and Technology*, 3 Bethesda Metro Center, Suite 1500, Bethesda, MD 20814.

Circulation
PDA
3 Bethesda Metro Center, Suite 1500
Bethesda, MD 20814
+1(301) 656-5900

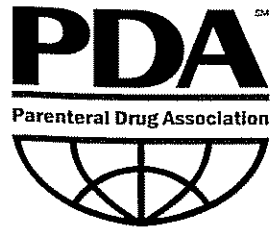
Advertising
Dorothea McGuire
+1(301) 656-5900 x150
mcguire@pda.org

Printed in the USA.

ISSN 1079-7440

Copyediting services provided by
Paul Casella, MFA
Iowa City, IA

Typesetting and other production services provided by
Cadmus Professional Communications
Ephrata, PA, USA



3 Bethesda Metro Center
Suite 1500
Bethesda, MD 20814 US
Tel: +1 (301) 986-0293
Fax: +1 (301) 986-0296
E-mail: info@pda.org
Web site: www.pda.org