

Technical Report No. 58

Risk Management for

Temperature-Controlled Distribution

2012



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PDA Risk Management for Temperature-Controlled Distribution

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The content and views expressed in this document are the result of a consensus achieved by the authorizing Task Force and are not necessarily views of the organizations they represent.

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Technical Report No. 58

ISBN: 978-0-939459-43-8

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Table of Contents

1.0 Introduction	1	5.3 Risk Insurance.....	25
2.0 Glossary of Terms	3	5.3.1 Incoterms®	25
2.1 Definition of Acronyms	6	5.3.2 Written Agreements and KPIs in the Supply Chain.....	26
3.0 Temperature-Controlled Distribution Management	7	5.4 Benefit-risk Analysis.....	27
3.1 Requirements	7	5.5 Summary.....	27
3.2 Design and Qualification.....	8	6.0 Risk Review	28
3.3 Quality Management System	10	6.1 Introduction.....	28
3.4 CAPA Management.....	11	6.2 Incident Management	28
3.5 Change Control.....	12	6.2.1 Definition of an Incident.....	28
3.6 Quality Risk Management	13	6.2.2 Responsibilities and Documentation.....	28
3.7 Temperature-Controlled Distribution Risk Management	15	6.2.3 Product Quality Impact Evaluation	29
4.0 Risk Assessment	16	6.2.4 Product Disposition.....	30
4.1 Introduction.....	16	6.2.5 Root Cause Analysis and Corrective Action/Preventive Action	30
4.2 Failure Modes and Effects Analysis.....	16	6.3 Vendor and Customer Complaints	31
4.2.1 Assign Team and lead for the FMEA Workgroup.....	17	6.4 Auditing.....	31
4.2.2 Map the Process	17	6.5 Trend Analysis.....	32
4.2.3 Assign ratings for severity, probability of occurrence and detection..	17	6.5.1 Periodic Review	32
4.2.4 Description of the Shipping Lane	17	6.5.2 Risk Factors.....	32
4.2.5 Execution of the FMEA	18	6.5.3 Temperature Data Interpretation	33
4.2.6 Risk Priority Number.....	20	6.5.4 Tools for Trend Analysis.....	34
4.2.7 Recommendation of Actions.....	20	7.0 Appendices	35
4.2.8 Recalculation of Risk Priority Number.....	20	7.1 FMEA Temperature-Controlled Truck	35
4.3 FMEAs for Five Shipping Scenarios.....	20	7.1.1 Lessons Learned.....	39
4.3.1 Temperature-Controlled Truck.....	21	7.2 FMEA Temperature-Controlled Ocean Container	40
4.3.2 Temperature-Controlled Ocean Container	22	7.2.1 Lessons Learned.....	44
4.3.3 Active ULD	22	7.3 FMEA Active Unit Load Device (ULD).....	44
4.3.4 Thermal Packout by Courier.....	22	7.3.1 Lessons Learned.....	50
4.3.5 Thermal Packout by Air.....	22	7.4 FMEA Thermal Pack-out by Courier.....	51
4.4 Summary.....	23	7.4.1 Lessons Learned.....	56
5.0 Risk Control	24	7.5 FMEA Thermal Pack-out by Air.....	56
5.1 Introduction.....	24	7.5.1 Lessons Learned.....	61
5.2 Risk Control Approaches	24	7.6 Incoterms® 2010 by the International Chamber of Commerce (ICC).....	61
5.2.1 Risk Avoidance.....	24	8.0 Additional Reading	64
5.2.2 Risk Mitigation	24	9.0 References	65
5.2.3 Risk Acceptance.....	25		
5.2.4 Risk Transfer.....	25		

FIGURES AND TABLES INDEX

Figure 3.0-1	Temperature-Controlled Distribution Management Model	7	Figure 7.2-3	FMEA Ratings Table	42
Figure 3.6-1	Quality Risk Management (from ICH Q9 Guideline)	14	Figure 7.2-4	FMEA Results Table (Top Five results) .	43
Figure 3.7-1	Temperature-Controlled Distribution Risk Management Model	15	Figure 7.2-5	FMEA Recommendations Table.....	43
Table 4.2.5-1	FMEA execution steps with sample answers to questions.	19	Figure 7.3-1	Key Scenario Information	45
Table 4.3-1	Five FMEA shipping scenarios	21	Figure 7.3-2	Process Map	46
Table 4.4-1	FMEA Highlights from five executed scenarios	23	Figure 7.3-3	FMEA Ratings Table	47
Table 6.2.2	Responsibility matrix outlining responsibility associated with an incident	29	Figure 7.3-4	FMEA Results Table (Top Five Results)	48
Figure 7.1-1	Key Scenario Information	35	Figure 7.3-5	FMEA Recommendations Table.....	49
Figure 7.1-2	Process Map	36	Figure 7.4-1	Key Scenario Information	51
Figure 7.1-3	FMEA Rating Table	37	Figure 7.4-2	Process Map	52
Figure 7.1-4	FMEA Results Table (Top Five Results)	38	Figure 7.4-3	FMEA Ratings Table	53
Figure 7.1-5	FMEA Recommendations Table.....	39	Figure 7.4-4	FMEA Results Table (Top Five Results)	54
Figure 7.2-1	Key Scenario Information	40	Figure 7.4-5	FMEA Recommendations Table.....	55
Figure 7.2-2	Process Map	41	Figure 7.5-1	Key Scenario Information	56
			Figure 7.5-2	Process Map	57
			Figure 7.5-3	FMEA Ratings Table	58
			Figure 7.5-4	FMEA Results Table (Top Five Results)	59
			Figure 7.5-5	FMEA Recommendations Table.....	60

1.0 Introduction

This technical report describes risk management for temperature-controlled distribution of pharmaceutical products. It is meant to assist stakeholders in the supply chain to preserve the quality, safety and efficacy of these products during distribution. This guidance document serves to complement the information provided in ICH Q9 guideline (Quality Risk Management) (1) and previously published PDA technical reports no. 39, 46, 52 and 53 (2,3,4,5) by assessing, controlling and reviewing risks with equipment, processes, people and external factors, like weather and natural disasters, during distribution.

1.1 Goal

The goals of risk management in the temperature-controlled distribution of pharmaceuticals, biological medical products and medical devices, hereafter referred to as (pharmaceutical) products, are to:

- Preserve the quality, safety and efficacy of the product
- Understand the distribution process
- Reduce risk
- Understand residual risk
- Improve the effectiveness of the process

The main questions are: What are the risks? How can we manage and mitigate them?

The risks involved in temperature-controlled distribution differ from manufacturing-related risks; rather than contributing to the manufacturing quality of the product, they center on the risk of product degradation. Good Manufacturing Practices (GMP) and Good Distribution Practices (GDP) ensure the quality and the efficacy of drug products and guard patient safety by protecting products from detrimental factors, the most prevalent of which in distribution is temperature. Because distribution resides outside the “four-walled compliance” of manufacturing and it is increasingly complex in an expanding global market, distribution risk management is essential. As such, industry-wide guidance on risk management and risk analysis for temperature-controlled distribution benefits pharmaceutical manufactures, supply chain partners, clinicians and patients.

This document provides specific guidance on the identification, assessment, evaluation, control and review of risks in the distribution process, such as receipt, storage, handling and shipping of bulk, intermediate and finished pharmaceuticals, biological medicinal products and medical devices. It also provides guidance for handling incidents, like temperature excursions, that occur during the distribution process.

This guidance has been developed by the PDA PCCIG Task Force on Risk Management for Temperature-Controlled Distribution, a group that includes representatives from the pharmaceutical industry, suppliers of active and passive shipping systems and temperature monitors, logistic service providers and carriers. This document is written for stakeholders in the pharmaceutical supply chain, including the manufacturer, supplier of active systems, supplier of passive systems, supplier of temperature monitors, logistic service provider, carrier, clinician, handling agent, airline and any other interested reader. It is assumed that the reader is familiar with the ICH Q9 guideline on Quality Risk Management as the same terminology is used in this document. Definitions of terms and acronyms are included in **Sections 2.0** and **2.1**, respectively.

Section 3.0 introduces a conceptual model for temperature-controlled distribution management. The Temperature-Controlled Distribution Management model addresses and characterizes five critical stages of temperature-controlled distribution including Requirements, Design and Qualification, Quality Management System, CAPA Management, and Change Control. The section ends with a

comparison of the model with the Quality Risk Management model from ICH Q9.

Section 4.0 focuses on risk identification, analysis and evaluation for active and passive shipping systems and temperature monitoring. It includes five examples of modes of transport, including temperature-controlled trucking, temperature-controlled ocean container, active Unit Load Device (ULD) and two types of thermal packouts. For each mode of transport, a sample risk assessment is provided using the Failure Modes and Effects Analysis (FMEA). This tool gives readers the opportunity to identify, analyze and evaluate risk, and assign a rating for each risk. The results are shared and discussed.

Section 5.0 deals with risk control. Here procedures are discussed to determine whether to mitigate or to accept a given risk using a science-based approach and benefit-risk analysis. It also describes and discusses risk insurance between stakeholders in the entire pharmaceutical supply chain. The point of view of an insurance company towards temperature-controlled distribution is presented and the capabilities of suppliers, logistics service providers, carriers, shippers and receivers to address risks are reviewed.

Section 6.0 pinpoints the risk review of events. It includes incident management, roles and responsibilities, detection and communication of events, root cause analysis, product disposition, CAPA management, and trend analysis on deviations. It also addresses risk factors in the supply chain, including risk in the detection of events, misinterpretation of data and miscommunication.

Appendices and references are at the end of the document. The appendices include examples of five executed FMEAs for the distribution of products in temperature-controlled containers and thermal packouts and a description of Incoterm[®] definitions.