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Guidance for Industry:
Stability Testing to
Support Distribution of
New Drug Products



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PDA Stability Testing to Support Distribution of New Drug Products

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Table of Contents

1.0 INTRODUCTION	2
1.1 Purpose	3
1.2 Scope	4
2.0 GLOSSARY OF TERMS	5
3.0 DRUG PRODUCT.....	6
3.1 General.....	6
3.2 Standard ICH Testing.....	6
3.3 The Role of Accelerated Testing	7
3.4 Additional Temperature-Stress Studies	7
3.4.1 Extreme Temperature Studies.....	8
3.4.2 Temperature-Cycling Studies.....	9
3.5 Non-Temperature Transportation Hazards.....	10
3.5.1 Shock (Drop) and Vibration.....	11
3.5.2 Air Pressure.....	11
3.5.2.1 Surface Shipments	11
3.5.2.2 Air Shipments	11
3.5.3 Humidity.....	11
3.6 Timing of Stability Testing to Support Drug Product Distribution	11
3.7 Evaluation and Determination of Time Out of Storage Recommendations and Stability Budget	12
4.0 BULK DRUG PRODUCT	21
5.0 CLINICAL TRIAL MATERIALS	22
6.0 REFERENCES	23

FIGURES AND TABLES INDEX

Table 1.1 Good Distribution Practices Pillars	3
Figure 3.1 Distribution Model.....	6
Table 3.2 Standard Stability Testing Conditions for Drug Product.....	7
Table 3.4.1-1 Example Extreme Excursion Studies for Pharmaceutical Drug Product.....	8
Table 3.4.1-2 Example Extreme Excursion Studies for Biological Drug Product.....	8
Table 3.4.2-1 Example Temperature-Cycling Studies for Pharmaceutical Drug Product	9
Table 3.4.2-2 Example Temperature-Cycling Studies for Biological Drug Product.....	10
Table 3.7-1 Time Out of Storage for a Frozen Drug Product (i.e., -20°C ± 10°C)	14
Table 3.7-2 Example Stability Budget for a Frozen Drug Product	15
Table 3.7-3 Time Out of Storage for a Refrigerated Drug Product	16
Table 3.7-4 Example Stability Budget for a Refrigerated Drug Product	17
Table 3.7-5 Time Out of Storage for a Room Temperature Drug Product.....	18
Table 3.7-6 Example Stability Budget for a Room Temperature Drug Product.....	20

1.0 Introduction

Stability testing is the primary type of testing necessary to provide data that will enable appropriate decisions regarding the conditions under which a finished material is to be stored, transported, and used. The International Conference on Harmonisation (ICH) published guidelines that address storage conditions, whereas this PDA Technical Report addresses stability studies to support distribution conditions. Shock and vibration testing also has a role, particularly in regard to transportation of liquid formulations of certain biologic molecules. This guidance will provide recommendations on the stability studies needed address the risks that face drug products in the distribution process, as well as supporting temperature excursions outside the long-term storage condition during storage.

This guidance focuses on four situations that should be considered during stability testing; these are:

1. **Product Storage:** Temperature is typically controlled and the risk of shock and vibration is expected to be minimal.
2. **Manufacturing and distribution operations (road, sea, and/or air):** Product is moved from one storage condition to another: temperature control may or may not be present. In addition to temperature stress, the risk of shock and vibration may be significant during distribution operations.
3. **Product Use under many circumstances, including following reconstitution from powder or simply by end-users (practitioners and/or patients):** There may be considerable variability in temperature control but the risk of shock and vibration is minimal.
4. **Excursions:** Temperature goes outside the recommended range for that segment of distribution or during controlled temperature storage of the product.

For products stored under frozen or refrigerated long-term conditions in situations 2 and 3 above, product may be exposed to temperature conditions outside the long-term storage condition during manufacturing, distribution and customer handling steps (e.g., bulk transport, filling and packaging operations, final product distribution operations, end user administration). The allowable exposure period and temperature range outside of the long-term storage condition is determined by accelerated stability data and can be further supported with the use of temperature stress and temperature-cycling stability data. When there is not a significant difference between long-term and accelerated stability study results, the allowable exposure period and temperature may be defined by the accelerated stability study (e.g., 6 months at 25°C for a 2-8°C product). However, if there is a significant difference in the stability data obtained between accelerated and long-term conditions, a shorter exposure period may need to be established based upon cumulative long-term and accelerated losses and meeting the required shelf life specifications. For products with limited exposure periods outside of the long-term storage conditions, tracking and control of product exposure periods becomes essential at each step of the process and distribution chain.

The allowable time and temperature conditions outside of the long-term storage condition for a material must be budgeted among competing needs such as additional manufacturing or packaging and labeling operations, transportation and the end user. This has been referred to as “time out of refrigeration,” “time out of storage,” or “time out of temperature.” For the purpose of this guidance, the phrase “time out of storage” will be used.

For situation 4, to support excursions that go beyond accelerated conditions or have a longer duration, additional studies above the accelerated conditions, freeze-thaw studies and temperature-cycling studies may be useful.

This guidance will also address the frequency, timing and extent of stability and shock and vibration testing needed to provide adequate support for appropriate label statements and to cover the four situations described above.