Regulatory Basis:
FDA Quality Systems Regulations

Reference: FDA CFR - Code of Federal Regulations Title 21

General Discussion
Some GMP sites may be practicing to ship some oral dosage form products from manufacturing facilities to Distribution Centers under controlled (defined temperature range) temperature conditions. Given the characteristics and stability performance of many solid oral dosage form products, shipment under a defined temperature range is not necessary. This document provides the scientific and risk management assessment process to support the evaluation and, where appropriate, discontinuation of solid oral dosage form shipment under defined temperature range conditions, dependent upon the results of individual product analyses.

Assumptions
1. During summer months and in tropical climates, pharmaceutical products being shipped under ambient conditions have the potential to be exposed to elevated temperatures reaching an approximate maximum temperature of 50ºC (122ºF).

2. Review of central America to United States Distribution Centres shipment time indicates that the typical shipment time for these pharmaceutical products from manufacturing facilities to distribution centers is less than two weeks.

   The presented rationale may be applied to discontinue defined temperature range shipments for other shipping routes if the shipment time is known and falls within the assumptions of this model.

3. Since the maximum exposure to elevated temperatures occurs during day time hours (approximately 12 hours per day), for a two week shipment time the actual exposure to elevated temperatures is estimated to be a maximum of one week as a worst case scenario.

4. Applicability of this document is limited to solid oral dosage forms (e.g. tablets, hard gelatin capsules, powders, etc.). Given dosage form characteristics, shipment of other dosage forms (e.g. soft gelatin capsules, liquid products, etc.) should be performed under temperature conditions in accordance with product labeling.

Requirements
1. A minimum of 3 months stability data at 40ºC/75%RH or 40ºC exists for product to be evaluated.

2. Prior to implementation of ambient shipment of a product currently shipped under defined temperature range conditions, a documented assessment confirming satisfactory (compliance with specifications) 3 month stability performance at the 40ºC/75%RH or the 40ºC condition is to be prepared. If available, the required stability information may be obtained from previously

Evaluation Process Supporting Elimination of Defined Shipment Temperature Range for Solid Oral Dosage Forms

Therefore, if satisfactory 3 month 40°C/75%RH or 40°C stability data are available for a product, shipment of the product under ambient temperature conditions is supported.

Additionally the impact of a product exposed to 50°C storage for 2 weeks, followed by storage at ambient temperature through various expiration periods was assessed with regard to mean kinetic temperature and summarized below:

Expiry	Weeks	25°C Storage	30°C Storage
		Mean Kinetic Temperature (MKT)	
18 months	78	27	31
24 months	104	27	31
30 months	130	27	31
36 months	156	26	31
48 months	208	26	31
60 months	260	26	30

Since a tolerance of +/- 2°C is acceptable for storage of drug product in stability chambers, changes in MKT greater than 2°C would indicate potential impact on stability performance over the expiry period. This analysis demonstrates that the impact of a 2 week 50°C excursion would not increase the MKT more than 2°C for expiration dates of at least 18 months; therefore, the impact on stability through expiry would be negligible.

Conclusion

This document provides the scientific and risk management assessment to demonstrate that solid oral dosage forms with acceptable (compliance with specifications) 3 month stability data at 40oC/75%RH or 40oC may be shipped under ambient temperature conditions. Additionally, it provides the requirements to implement ambient shipping for those applicable products that currently are shipped under defined temperature range conditions

