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Transporting Life

First Annual

Frozen Shipping Summit

December 1-2, 2011

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AN OVERVIEW OF GLOBAL HANDLING, STORING AND SHIPPING OF TEMPERATURE SENSITIVE PRODUCTS

CryoPort First Annual Frozen Shipping Summit
December 1, 2011

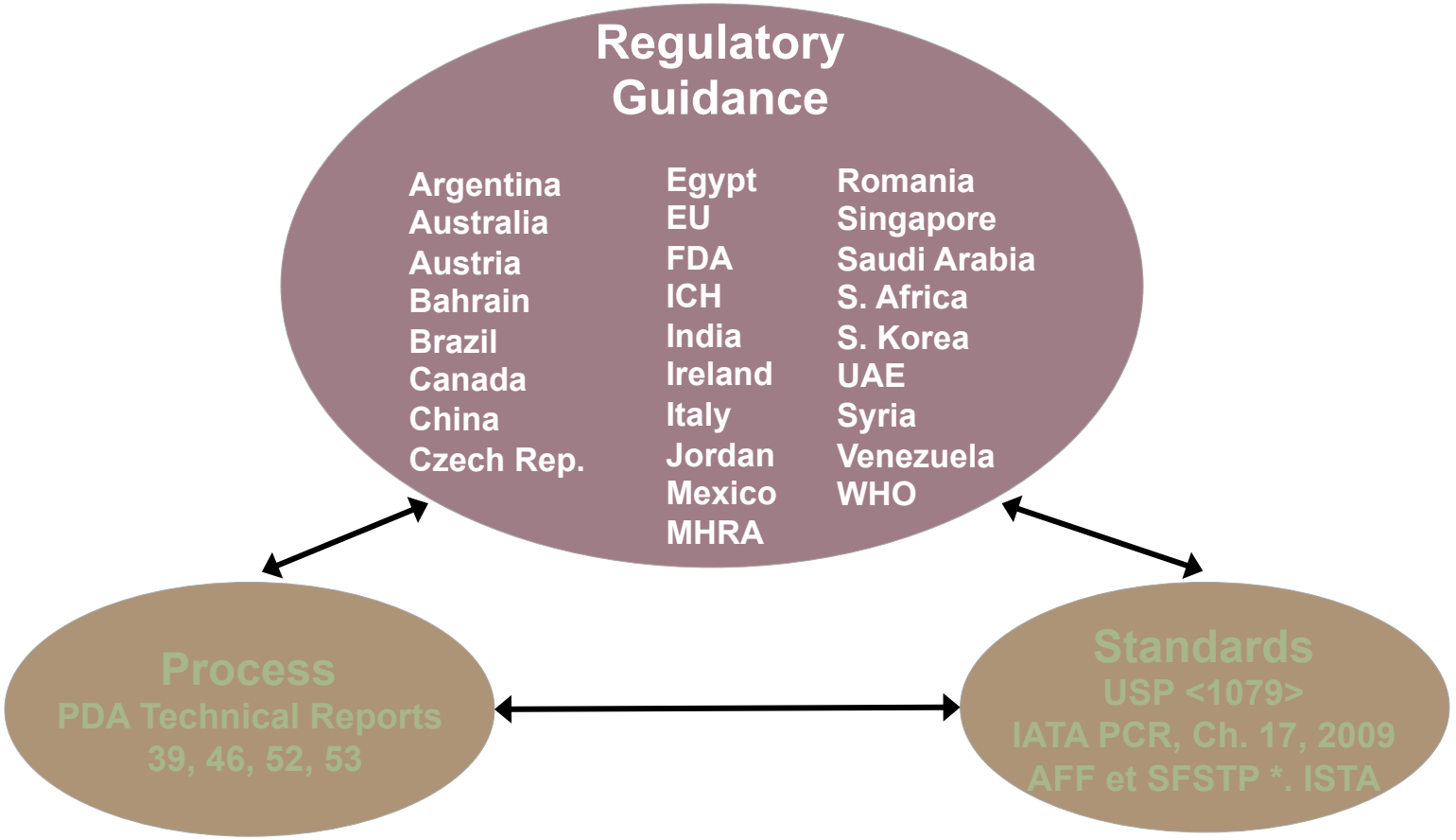
Presented by
Rafik H. Bishara, Ph.D.
Technical Advisor

Agenda

- Regulations and Guidelines
- Innovations
- Q&A

REGULATIONS

Regulatory and Standards-Based Guidance



* Guide Pratique: Chaine du froid du medicament

Reference: Rafik H. Bishara, "The Impact of USP <1079> on Cold Chain Management", March 7, 2006 (Sensitech Sponsored Webinar), Revised October 28, 2011

PDA Technical Reports

PDA TR 39 (revised 2007) Guidance for Temperature-Controlled Medicinal Products: Maintaining the Quality of Sensitive Medicinal Products Through the Transportation Environment

PDA TR 46 Last Mile: Guidance for Good Distribution Practices for Pharmaceutical Products to the End User

PDA TR 52 Guidance for Good Distribution Practices (GDPs) for the Pharmaceutical Supply Chain

PDA TR 53 Guidance for Industry: Stability Testing to Support Distribution of New Drug Products

Good Distribution Practices (GDP) for the Pharmaceutical Supply Chain

First Mile **(Manufacturing, Storage, Shipping)**

Last Mile **(Distribution, Product to Patient)**

Manufacturer

- ❑ Highly Regulated (GMP)
- ❑ Multiple Resources for Guidance
- Technical Report 39
- USP
- World Wide GDP Regulations (variations)

Storage, Shipping, and Distribution

- ❑ Various Levels of Regulation (GDP)
- ❑ Numerous Routes for Transport
- ❑ Variation in Temperature Exposure
- ❑ Variation in Transit Time
- ❑ Variation in tools available to Monitor Quality

Health Care Professional

- ❑ Limited Data Available for assessing product exposure
- ❑ Variations in Excursion Management
- ❑ Packaging Inserts
- ❑ Warning Labels
- ❑ USP (1079)
- ❑ USP Monographs & Chapters
- ❑ Technical Report 39
- ❑ CDC and WHO

Patient

- ❑ Label instructions; guidance by physicians, nurses, and pharmacists

Preserve Product Integrity

Technical Report 52

PDA Technical Report No. 52

- Guidance for Good Distribution Practices (GDPs) for the Pharmaceutical Supply Chain
  - Describes the overall Quality System for distribution of pharmaceutical products
  - Meant to assist manufacturers in assuring that the quality, integrity, and efficacy of the product are not compromised in the distribution channels, including handling, storage, transportation and distribution.
  - Applies to all parties involved in the distribution channels, including but not limited to the holder of the marketing authorization, third party logistics service providers (3PLs), wholesale distributors, and transportation carriers
  - Date of Publication: August 2011

PDA Technical Report No. 52 (Cont'd.)

- Introduction
- Glossary of Terms
- Requirements
  - Stability
  - Distribution Control Management
  - Performance Management
  - Supply Chain Partner Management
  - Business Review Meetings

PDA Technical Report No. 52 (Cont'd.)

- Appendix – Good Storage and Shipping Checklist

A. Accreditation and Licensure

B. Quality System Comments

C. Building and Housekeeping

D. Pest Control

E. Product Storage

F. Temperature Control / Calibration Storage

G. Temperature Control Distribution

H. Inventory Control

I. Product Distribution

J. Systems

K. Insulated Shipping Systems

L. Carrier Transportation Temperature Control

M. Customer Returns

N. Complaints

O. Counterfeit and Tampering

P. Material / Product Description

Q. General

R. Training

S. Safety

PDA Technical Report 53

Technical Report No. 53

- Guidance for Industry: Stability Testing to Support Distribution of New Drug Products
- Describes and justify the studies using scientific data and rationale necessary to determine an appropriate stability budget for a drug product
- Focuses on four situations that should be considered during stability testing:
  - Product storage
  - Manufacturing and distribution operations (road, sea, and / or air)
  - Product use under many circumstances, including following reconstitution from powder or simply by end-users (practitioners and / or patients)
  - Excursions
  - Date of Publication: August 2011

Technical Report No. 53 (Cont'd.)

- Introduction
- Glossary of Terms
- Drug Product
- Bulk Drug Product
- Clinical Trial Material
- References

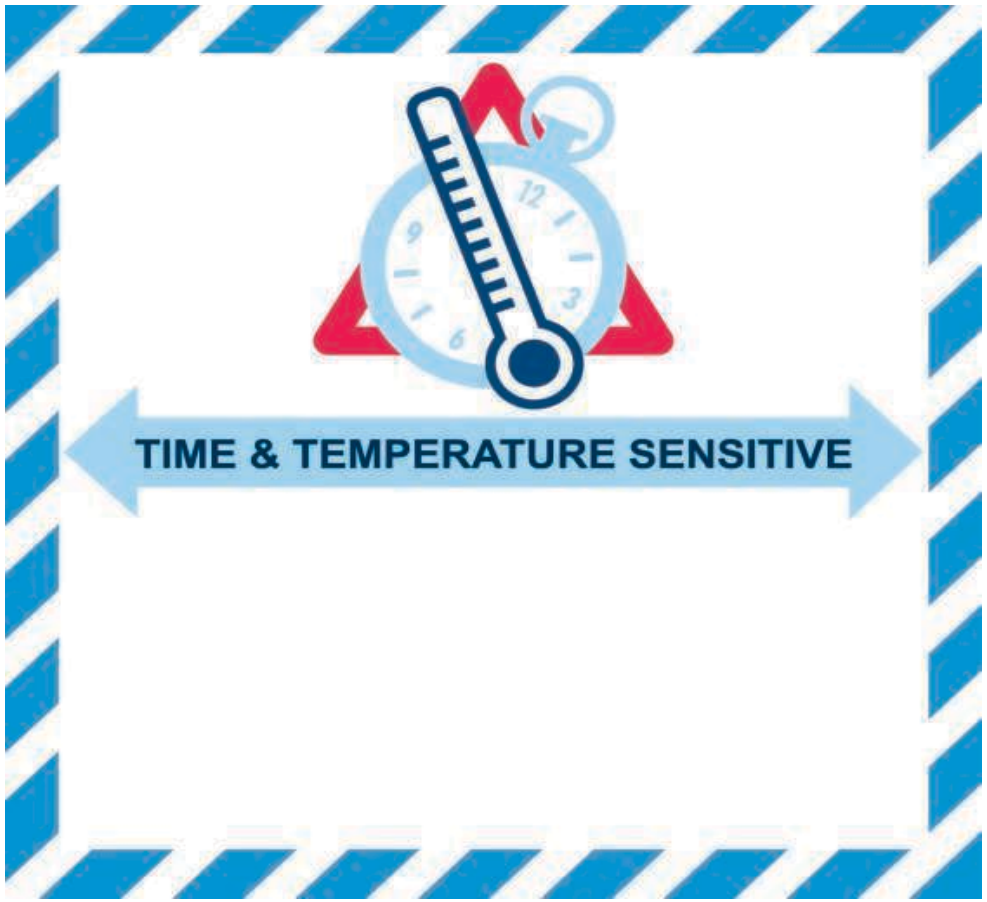
Technical Report No. 53 (Cont'd.)

- Tables
  - Standard Stability Testing Conditions for Drug Product
  - Example for Studies for Pharmaceutical and Biological Drug Products
    - Extreme Excursion
    - Temperature-Cycling
  - Time out of Range for Frozen (-20 degree C +/- 10 degree C), Refrigerated, and Room Temperature Drug Products
  - Example for Stability Budget for Frozen, Refrigerated and Room Temperature Drug Products

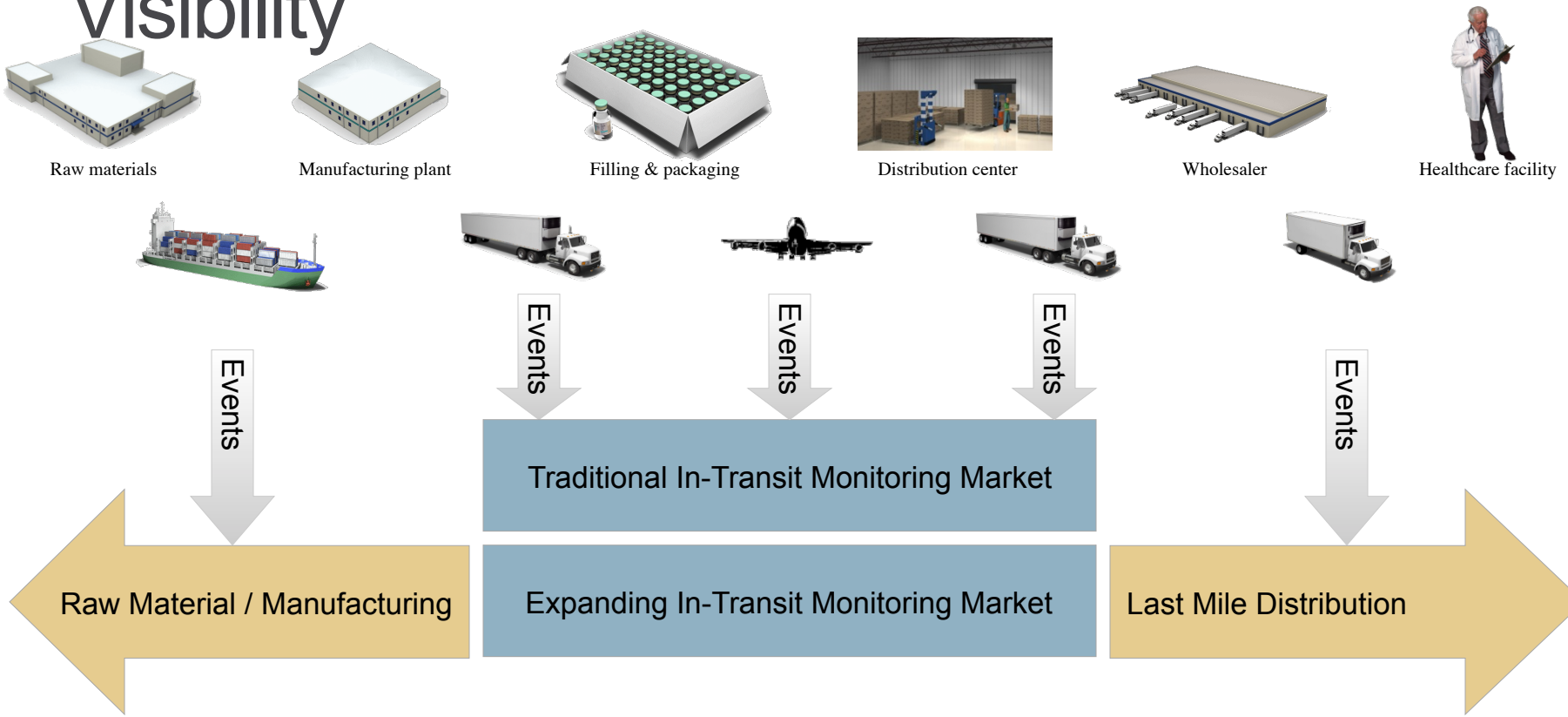
From GMP to GDPs – New Regulations

- Good Manufacturing Practices (GMPs) have been around (and modified/updated) for ~3 decades
- There are many G“X”Ps
  - GMP – Good Manufacturing Practices
  - GLP – Good Laboratory Practices
  - GCP – Good Clinical Practices
  - You may see cG“X”P
    - “c” stands for current, current is base of “audits”
    - Compliance by audits / regulatory enforcement
  - The logical extension of the Good “X” Practices into the supply chain are the GSPs and GDPs

IATA Label Revised October, 2009



Regulatory Guidance Pushing Cold Chain Visibility



USP General Chapter <1079> Published August 1, 2005

"Manufacturers and Distributors should work together to establish proper distribution and product-handling requirements for the purpose of ensuring appropriate product maintenance in transit."

What are Inspectors Looking for During the Regulatory Process?

- Standard Operating Procedures (SOPs)
- Temperature monitoring in warehouse
- Validation of freezer and refrigerators
- Product storage conditions
- Temperature control during transport
- Procedure for investigations and actions in the case of temperature excursion from the set parameters

Reference: Vincent Tong, HPFB Inspectorate, IPA Montreal, November 20, 2006

You can delegate authority,

but…

you cannot relinquish your responsibility

INNOVATIONS

Areas of Focus

- Packaging
  - Phase Change Material (PCM)
  - Containers
- Data monitoring
  - Data analysis
    - Quality decision supported by data
- A New Process
  - Depot Concept
  - Flexibility to cope with fast changing playing field

Current Challenges

- Track and Trace/ Pedigree
- Anti-counterfeiting, Tampering, Diversion Measures
- Global Security
- New Technology
  - RFID
  - Bar Coding
  - GPS
  - Real Time Data
  - Outsourcing
  - Due Diligence – The Audit Process

Questions?

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