

# Developing Temperature Controlled Environmental Test Standards

**Eric Joneson**

**Vice President, Lansmont Corporation**

**Executive Vice President, ISTA**

**Ed Church**  
Executive Director  
ISTA

**Don Wilson**  
Sr. Mgr. Engineering  
Amgen, Inc.

**Bill Lewis**  
Sr. Assoc. Project Mgmt.  
Amgen, Inc.

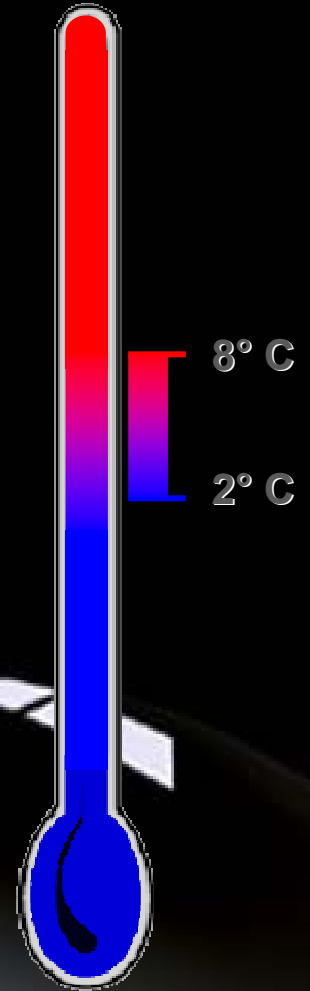
**Paul Harber**  
Assoc. Eng. Consultant  
Eli Lilly and Company



- **ISTA's initiative is to develop testing profiles for the Cold Chain transportation environment to meet qualification needs.**
- **Pharmaceutical Cold Chain Interest Group within the Parenteral Drug Association (PDA).**
- **Establish how industry approved testing profiles can be generated from sufficient environmental data that is then analyzed using accepted scientific practices.**
- **"If you can measure it – you can develop it!"**

# What is “Cold Chain?”

- Temperature Controlled supply chain
- Uninterrupted series of storage and distribution which maintains a given temperature range
- Common in pharmaceutical and biologics is the 2°C to 8°C range.



# All Packages Get Tested Against Why Do We Need a Lab Test?

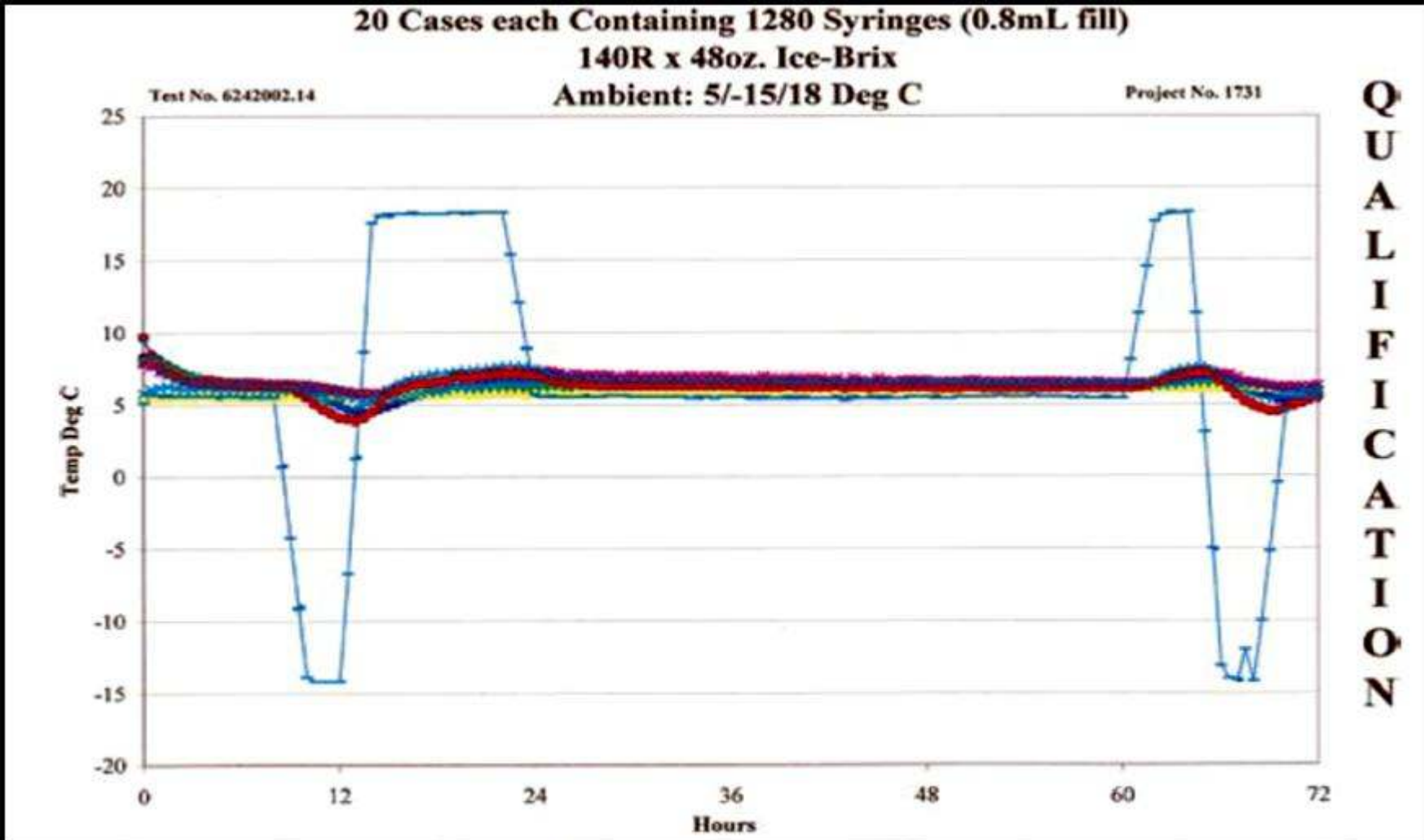


**Extreme Cold**

**Extreme Hot**



# Why Do We Need a Lab Test?





# Temperature Profile

**"Anticipate ambient temperature variations and duration to which a product "maybe exposed during transportation."**



## **PDA Technical Report No. 39**

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

prepared by **PCCIG**.

This Technical Report **provides guidance to both the pharmaceutical industry and regulators on the essential principles and practices for shipment of products which require controlled temperatures** during transit while providing a design approach to the development of specialized packages and systems which will protect temperature-sensitive products during transportation.

# Purpose of the ISTA Protocol

- Record the ambient temperature and humidity data that outbound packages are exposed to during typical United States shipments.
- Data to create a composite profile tool representative of the typical conditions encountered by packages during these shipments.
- Profiles will be used to statistically recreate the exposure conditions for lab qualification testing of transport packaging.

# Scope

- **Sending specially constructed data recording packages in triplicate on “round trip” shipments made within the continental U.S.**
- **Shipments originating at the Midwestern hubs of FedEx and UPS.**
- **Shipments will be to cities and towns that have FedEx and UPS “storefronts” within the vicinity of major wholesalers.**
- **Two seasonal campaigns:**
  - warmest and coldest extreme months of ambient temperatures and humidity data.



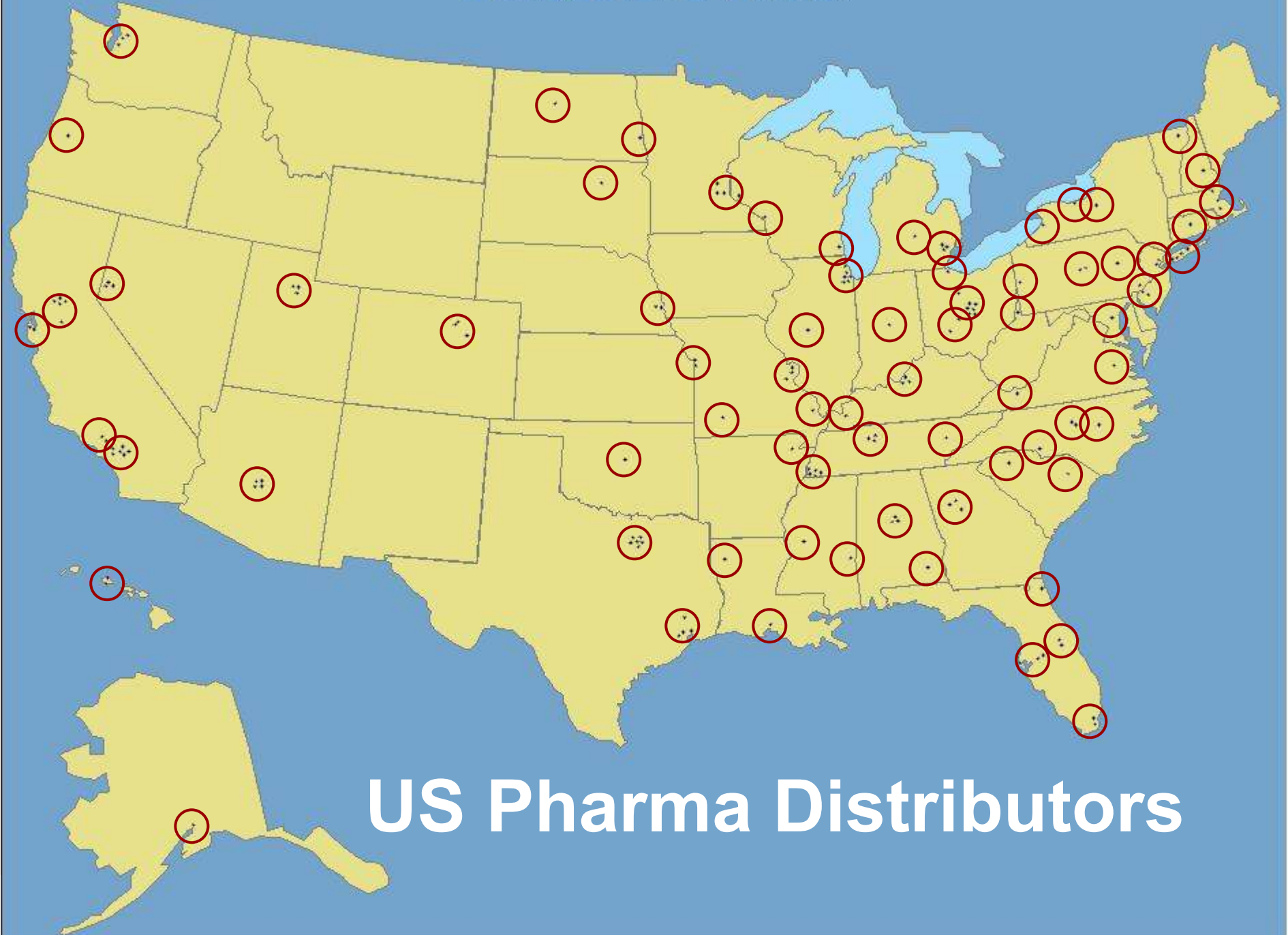
# Scope

- **Selection criteria of the shipments**
  - proximity of a wholesaler
  - availability of a nearby storefront at which to return the data recording packages to the hubs.
- **Outbound termination points determined**
  - consultation with the freight companies
  - referencing the climactic data as it is presented in the ASHRAE book of Fundamentals.

# Shipping Lane Determination

- Evaluated the major pharmaceutical wholesaler locations in the United States.
- UPS and FDX storefront locations were substituted to match the approximate air mileage for the initial shipment.
- After the initial air shipment, a ground shipment is needed to collect more temperature and humidity data.
  - additional UPS and FDX storefront locations were located between 200 to 300 miles away from the initial shipment point.
- Once shipments reach the end user locations, the shipments will be returned following the same route.

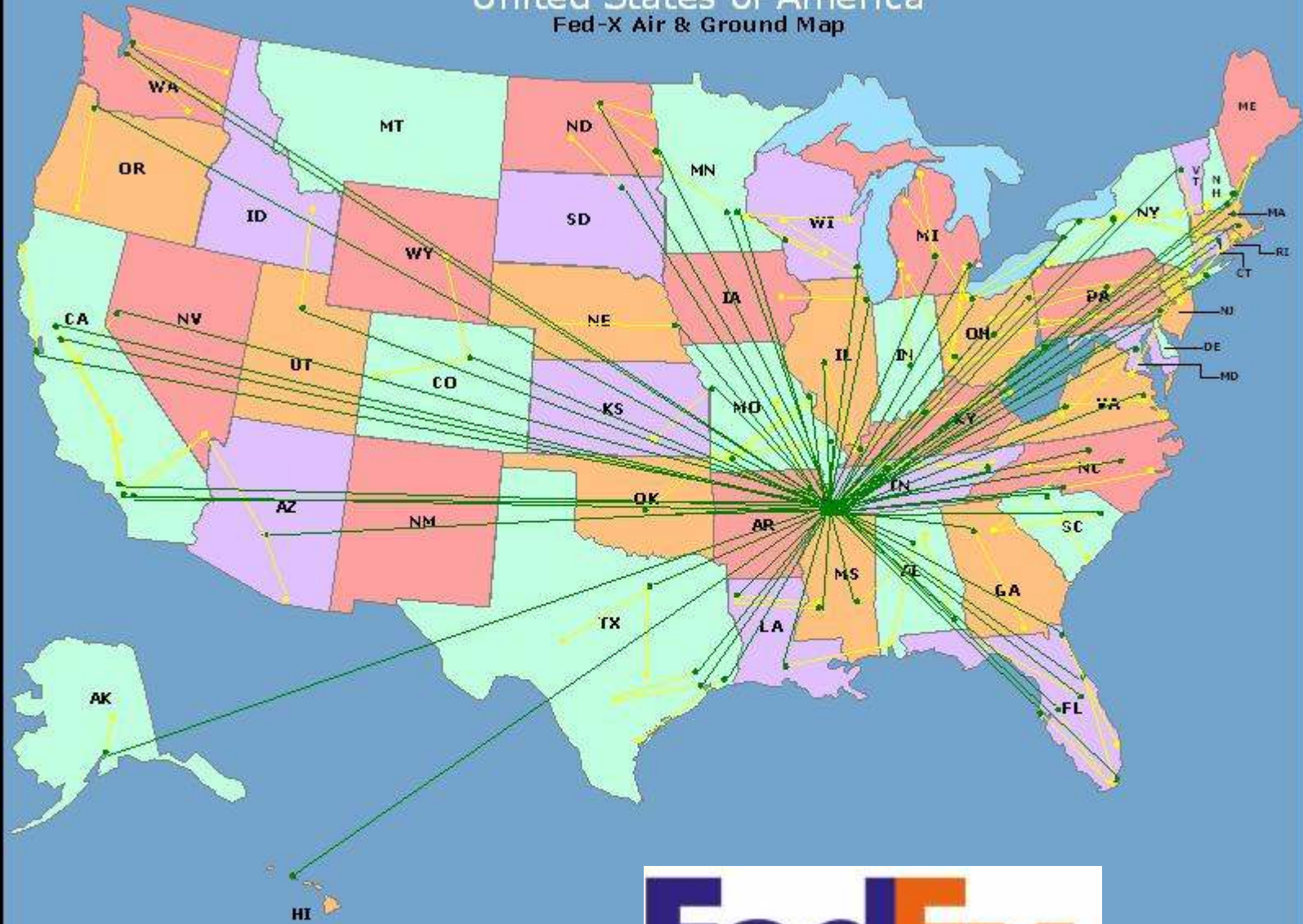
United States of America



**US Pharma Distributors**

# United States of America

## Fed-X Air & Ground Map



- = Fed-X Hub
- = Fed-X Ground Stores
- = Fed-X Ground Routes
- = Fed-X Air Stores
- = Fed-X Air Routes

**FedEx**



# FedEx®

# Air Hub to Air Store (156)

Shipping Point: FDX - Main Air Hub



| Address           | City    | State | Zip Code |
|-------------------|---------|-------|----------|
| 2903 Sprankle Ave | Memphis | TN    | 38118    |

Ship To: FDX Air Store

| Ship # | Address                | City       | State | Zip Code | Mileage |
|--------|------------------------|------------|-------|----------|---------|
| 1      | 300 E Dimond Blvd      | Anchorage  | AK    | 99515    | 4130    |
| 2      | 134 Woodburn Dr        | Dothan     | AL    | 36305    | 421     |
| 3      | 3260 Galleria Circle   | Hoover     | AL    | 35244    | 241     |
| 4      | 1901 6th Ave N         | Birmingham | AL    | 35203    | 228     |
| 5      | 3260 Galleria Circle   | Hoover     | AL    | 35244    | 421     |
| 6      | 2005 E Nettleton Ave   | Jonesboro  | AR    | 72401    | 83      |
| 7      | 201 E Washington St    | Phoenix    | AZ    | 85004    | 1540    |
| 8      | 9925 W McDowell Rd     | Avondale   | AZ    | 85323    | 1556    |
| 9      | 4150 N Drinkwater Blvd | Scottsdale | AZ    | 85251    | 1523    |
| 10     | 9925 W McDowell Rd     | Avondale   | AZ    | 85323    | 1556    |



# Air Hub to Ground Store (156)

Shipping Point: FDX - Main Air Hub



| Address           | City    | State | Zip Code |
|-------------------|---------|-------|----------|
| 2903 Sprankle Ave | Memphis | TN    | 38118    |

Ship To: FDX Ground Store

| Ship # | Address                     | City           | State | Zip Code | Mileage |
|--------|-----------------------------|----------------|-------|----------|---------|
| 1      | 418 3rd St, STE 7           | Fairbanks      | AK    | 99701    | 367     |
| 2      | 108 Rainbow Industrial Blvd | Rainbow City   | AL    | 35906    | 252     |
| 3      | 3691 Airport Blvd           | Mobile         | AL    | 36608    | 252     |
| 4      | 3691 Airport Blvd           | Mobile         | AL    | 36608    | 264     |
| 5      | 3691 Airport Blvd           | Mobile         | AL    | 36608    | 252     |
| 6      | 2525 Missouri Blvd # E      | Jefferson City | MO    | 65109    | 272     |
| 7      | 671 Mall Ring Circle        | Henderson      | NV    | 89014    | 284     |
| 8      | 4062 E Industry Dr          | Sierra Vista   | AZ    | 85635    | 203     |
| 9      | 671 Mall Ring Circle        | Henderson      | NV    | 89014    | 294     |
| 10     | 4062 E Industry Dr          | Sierra Vista   | AZ    | 85635    | 203     |

## UPS Air & Ground Map



# Typical Use of Carriers

- **FedEx and UPS are the dominant primary carriers used by pharmaceutical companies in the continental United States**
- **All 50 states are serviceable via 2nd Day Air service**
- **Additionally, ground services are available.**

# Temperature Information

- **ASHRAE historical temperature data**

American Society of Heating, Refrigerating and Air-Conditioning Engineers

- Compared against wholesaler locations in the USA

- determined the months that experienced the warmest and coldest extreme of ambient temperature.

- **It was determined that the average**

- hottest month is July

- coldest month is January.

# ASHRAE Climatic Data

American Society of Heating, Refrigerating and Air-Conditioning Engineers (ASHRAE) book of Fundamentals

| Ship # | Wholesaler City (ASHRAE) | State | Coldest Month | Temp °C | Hottest Month | Temp °C |
|--------|--------------------------|-------|---------------|---------|---------------|---------|
| 1      | ANCHORAGE                | AK    | January       | -23.7   | July          | 21.4    |
| 2      | DOTHAN                   | AL    | January       | -2.8    | July          | 35.3    |
| 3      | PELHAM (BIRMINGHAM)      | AL    | January       | -7.4    | July          | 35.1    |
| 4      | BIRMINGHAM               | AL    | January       | -7.4    | July          | 35.1    |
| 5      | MCCALLA (BIRMINGHAM)     | AL    | January       | -7.4    | July          | 35.1    |
| 6      | PARAGOULD (JONESBORO)    | AR    | January       | -11.6   | July          | 35.9    |
| 7      | PHOENIX                  | AZ    | December      | 2.9     | July          | 43.4    |
| 8      | TOLLESON (PHOENIX)       | AZ    | December      | 2.9     | July          | 43.4    |
| 9      | SCOTTSDALE (PHOENIX)     | AZ    | December      | 2.9     | July          | 43.4    |
| 10     | TOLLESON (PHOENIX)       | AZ    | December      | 2.9     | July          | 43.4    |



# Data Collection

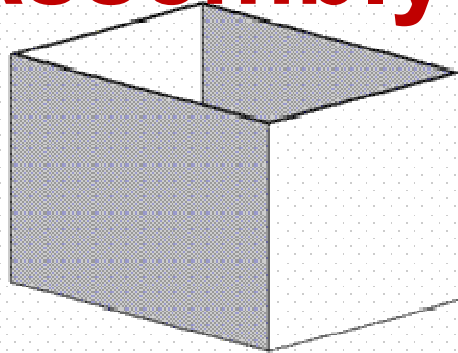
- Each shipment will record the ambient temperature and humidity data seen throughout the course of the shipment.
- Upon receipt of all the shippers, the data will be downloaded
- A hot and cold temperature and humidity profile will be created.

# Shipper

- The shipper's will mimic the size and weight of an actual shipment
- All of the shippers will be of the same size and weight
- Shipper's will be of a unique color for simplicity in identification.

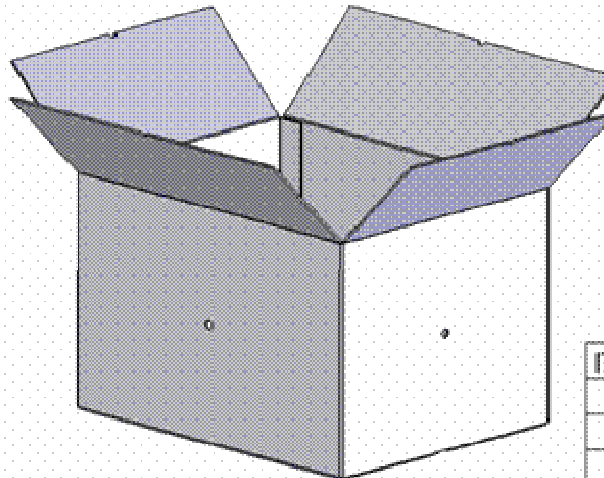
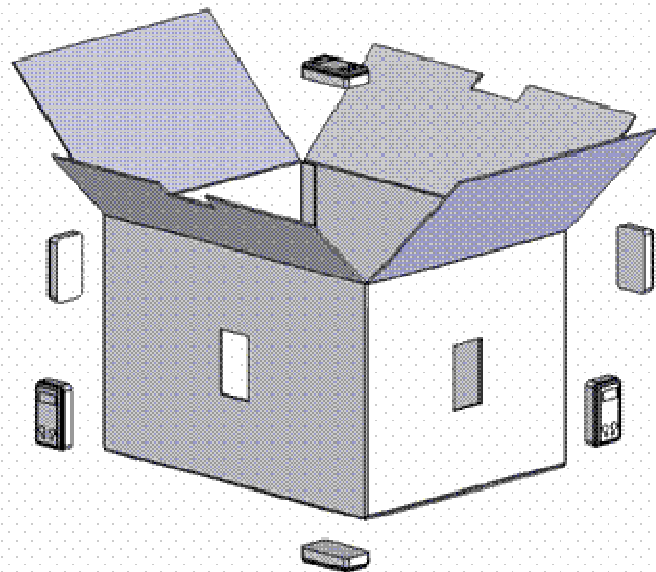


# Assembly Instructions for T.A.S.H.



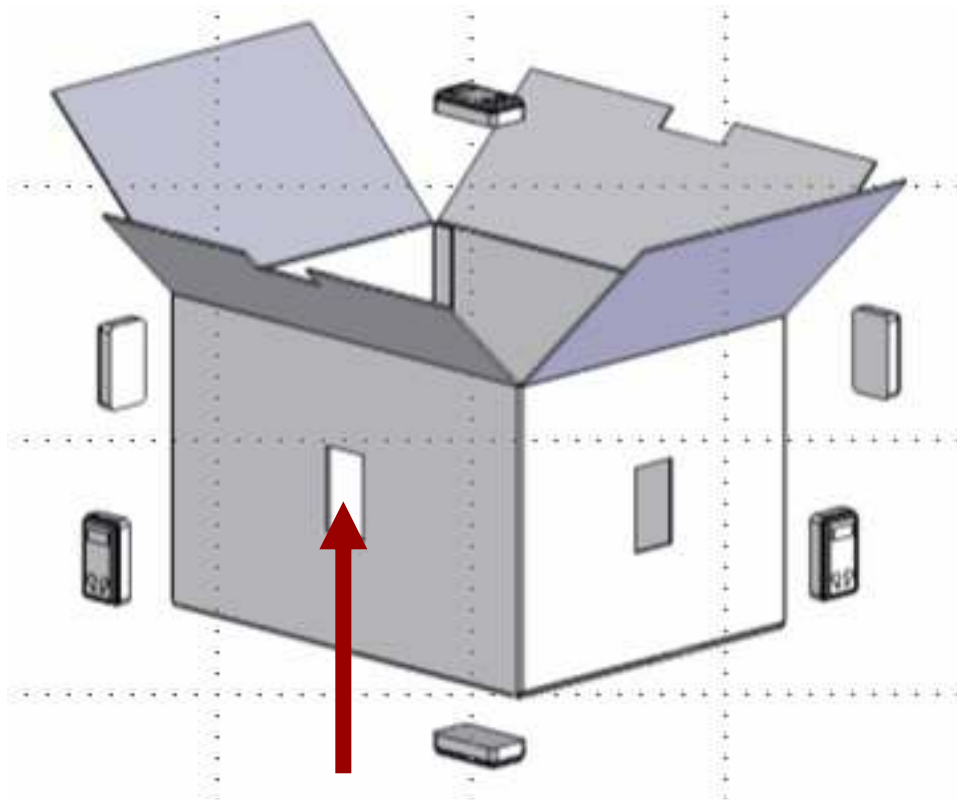
## Assembly Instructions

- 1) Insert TASH Tube into TASH CSSC
- 2) Close TASH CSSC
- 3) Insert 6 TempTale 4's into the TempTale holes of the TASH CSSC. Ensure the TempTale face is facing out
- 4) Activate the TempTale 4's
- 5) Insert the TASH CSSC into the TASH C1055 Box
- 6) Close and seal the TASH C-155 Box. Ensure Holes in TASH C-155 are not covered with tape.



## Temperature Acquisition Shipper (TASH)

| ITEM | QTY. | SPEC. NO. | PART NAME.      |
|------|------|-----------|-----------------|
| 1    | 1    |           | TASH C-155 Box  |
| 2    | 1    |           | TASH CSSC C-155 |
| 3    | 1    |           | TASH Tube C-155 |
| 4    | 6    |           | TempTale 4      |

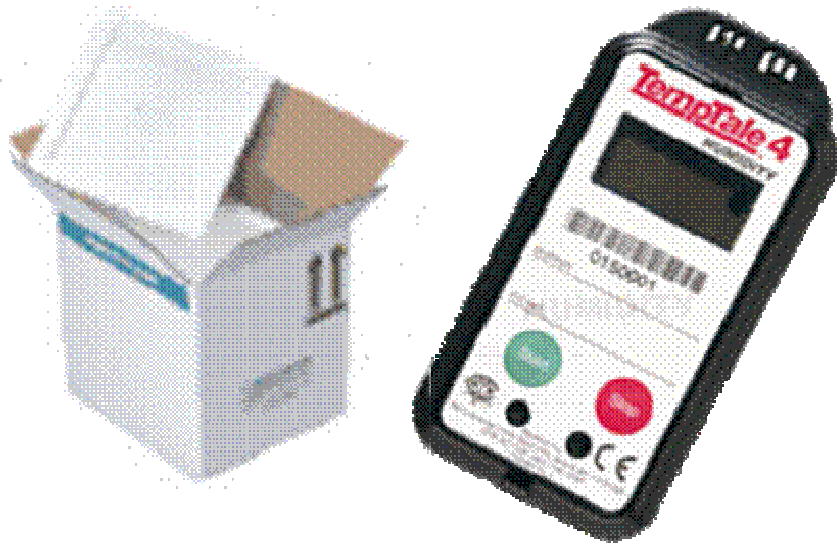


6 recessed in the box, but exposed to ambient temperature and humidity



# Temperature Profile Protocol

- Ship 3 Lanes, same day and same time
- Study starts  $\approx$  1/08 (6+ Months)
- 6 recorders in a box





# Temperature Profile Protocol

- **Destinations: Wholesalers**
- **Carriers: UPS and FedEx**
- **Some % of trips monitored for Shock, Drops and Vibration**



- **Scan to Scan**
- **Truck and Air**
- **Various sorts and hub conditions**

# Procedure

**The following are step by step procedures to be followed in the study.**

- 3.1 Assemble TASH shipper per ISTA procedure - 007.**
- 3.2 Label, launch, and insert every TempTale® 4 – Humidity Monitors into TASH Shipper (e.g. Lane 1, UPS, 1 of 3)**
- 3.3 Close and seal each TASH Shipper with tape (Sealing Tape, 3 in.) There is a Package Component Specification ISTA – 014 written.**
- 3.4 Label each TASH shipper with lane number, carrier, and shipment number (e.g. Lane 1, UPS, 1 of 3)**
- 3.5 Attach a document pouch to each TASH Shipper and secure with tape**
- 3.6 Attach a routing shipment log sheet / checklist to each TASH Shipper and insert into document pouch and seal.**
- 3.7 Create a shipping label and attach to TASH Shipper**
- 3.8 Stage and palletize completed TASH Shippers until all shippers have been packed out and labeled appropriately**
- 3.9 Execute shipments**
- 3.10 Upon receipt of TASH Shippers:**
  - Complete the routing shipment log sheet / checklist each TASH Shipper.
  - Open each TASH shipper
  - Stop TempTale® 4 – Humidity Monitors  
(DO NOT DISASSEMBLE TASH SHIPPERS)
  - Stage and palletize completed TASH Shippers until all shippers have been received
- 3.11 Ship all TempTale® 4 – Humidity Monitors to Sensitech for downloading data**
- 3.12 Download, save, and print all data from TempTale® 4 – Humidity Monitors**
- 3.13 Fill out a Data Sheet for each TempTale® 4 – Humidity Monitors and attach hard copies of the data to each sheet**
- 3.14 Send data to University of Florida to create hot and cold temperature and humidity profile standards**
- 3.15 Send Profiles to ISTA to incorporate in ISTA 7D and publish newly**

# Data Tracking Sheet

|                                                                        |                                                                                    |                                          |                                                                                     |
|------------------------------------------------------------------------|------------------------------------------------------------------------------------|------------------------------------------|-------------------------------------------------------------------------------------|
| Destination                                                            | CITY, ST                                                                           | Ship To:                                 | FedEx Store                                                                         |
| Origin NWS forecast high                                               | 74 °F                                                                              | • Name:                                  | • Street                                                                            |
| Shipment Type                                                          | Ground - <b>Air</b>                                                                | • Address:                               | • City, ST, ZIP                                                                     |
| Shipment Type                                                          |                                                                                    | • City, ST, ZIP:                         |                                                                                     |
| Create Return Label                                                    |   |                                          |                                                                                     |
| Temptale Serial Number                                                 | 143134141412341                                                                    | Temptale Received                        |  |
| Temptale Programmed                                                    |   | Confirm serial number                    |  |
| Temptale Activated                                                     |   | Download Data                            |  |
| Container Packed with Temptale, Instructions, and Return Label, Sealed |  | Filename<br>INDCT_{destination} __MM__YY | IND_CITY_08_05                                                                      |
| Staged at Dock (time)                                                  | 11:30                                                                              | File Location                            | Server Name and folder                                                              |
| Initials/Date for shipment                                             | SMS 08-AUG-2005                                                                    | Initials/Date for Receipt                | SMS 12-AUG-2005                                                                     |

# Routing Shipment Log Sheet

| Lane Number                         | Shipper Number | Carrier |
|-------------------------------------|----------------|---------|
|                                     |                |         |
| <b>Temptale® 4 Humidity Monitor</b> |                |         |
| #                                   |                |         |
| #                                   |                |         |
| #                                   |                |         |
| #                                   |                |         |
| #                                   |                |         |
| #                                   |                |         |
|                                     |                |         |
| Shipment Prepared By:               |                |         |
| Date:                               |                |         |
|                                     |                |         |

# Routing Shipment Check List

| Shipment<br>Leg Number | Shipment Addresses |                                                      | Received By:<br>Initial/Date |
|------------------------|--------------------|------------------------------------------------------|------------------------------|
| Mode of<br>Transport   |                    |                                                      |                              |
| <b>1</b>               | <b>From:</b>       | 6406 Grade Lane, Louisville, KY. 40213               |                              |
| <b>Air</b>             | <b>To:</b>         | 205 E. Dimond Blvd, Anchorage, AK. 99515             |                              |
| <b>2</b>               | <b>From:</b>       | 205 E. Dimond Blvd, Anchorage, AK. 99515             |                              |
| <b>Ground</b>          | <b>To:</b>         | 607 Old Steese Hwy Ste. B, Fairbanks, AK. 99701-1706 |                              |
| <b>3</b>               | <b>From:</b>       | 607 Old Steese Hwy Ste. B, Fairbanks, AK. 99701-1706 |                              |
| <b>Ground</b>          | <b>To:</b>         | 205 E. Dimond Blvd, Anchorage, AK. 99515             |                              |
| <b>4</b>               | <b>From:</b>       | 205 E. Dimond Blvd, Anchorage, AK. 99515             |                              |
| <b>Air</b>             | <b>To:</b>         | 6406 Grade Lane, Louisville, KY. 40213               |                              |

# Execution Plan

Wholesaler List / ASHRA  
USA with Lane #'s  
Report  
ISTA-001  
Dave Moore / Bill Lewis

UPS Routing and Store Fronts  
Report  
ISTA-002  
Bill / Dave Moore

FedEx Routing and Store  
Fronts  
ISTA-003  
Bill Lewis/ Dave Moore

Forms for  
156 Lanes  
ISTA-005  
Dave Moore

Comparison of Color  
Report  
Brian Wallin

Instructions for  
Transporter  
ISTA-004  
Paul Harber

TASH  
Specification  
ISTA-006  
Brian Wallin

TASH Data Analyses  
Report  
ISTA-008  
Chris Corey

TempTale  
Specification  
ISTA-011  
Dave Ray

Shipping Boxes for TempTales  
Specification  
ISTA-013  
Bill Lewis

3" Tape Specification  
ISTA-014  
Brian Wallin

Execution Plan  
Don Wilson  
ISTA-015

TASH SOP  
ISTA-007  
Brian Wallin

Lane Reports / Instructions  
ISTA-009  
Chris Corey

TempTale  
Activation Specification  
ISTA-012  
Dave Ray

Lane / Profile Data Analyses  
Report  
ISTA-010  
Ray Cowland

ISTA-016  
Protocols  
Bill Lewis and Paul Harbor

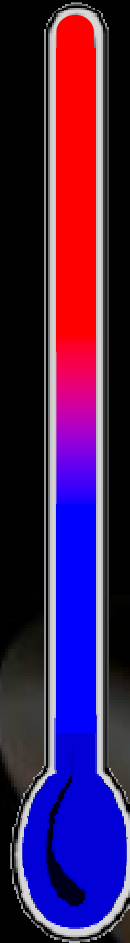
Schedule  
Don Wilson

Cost Report  
Don Wilson

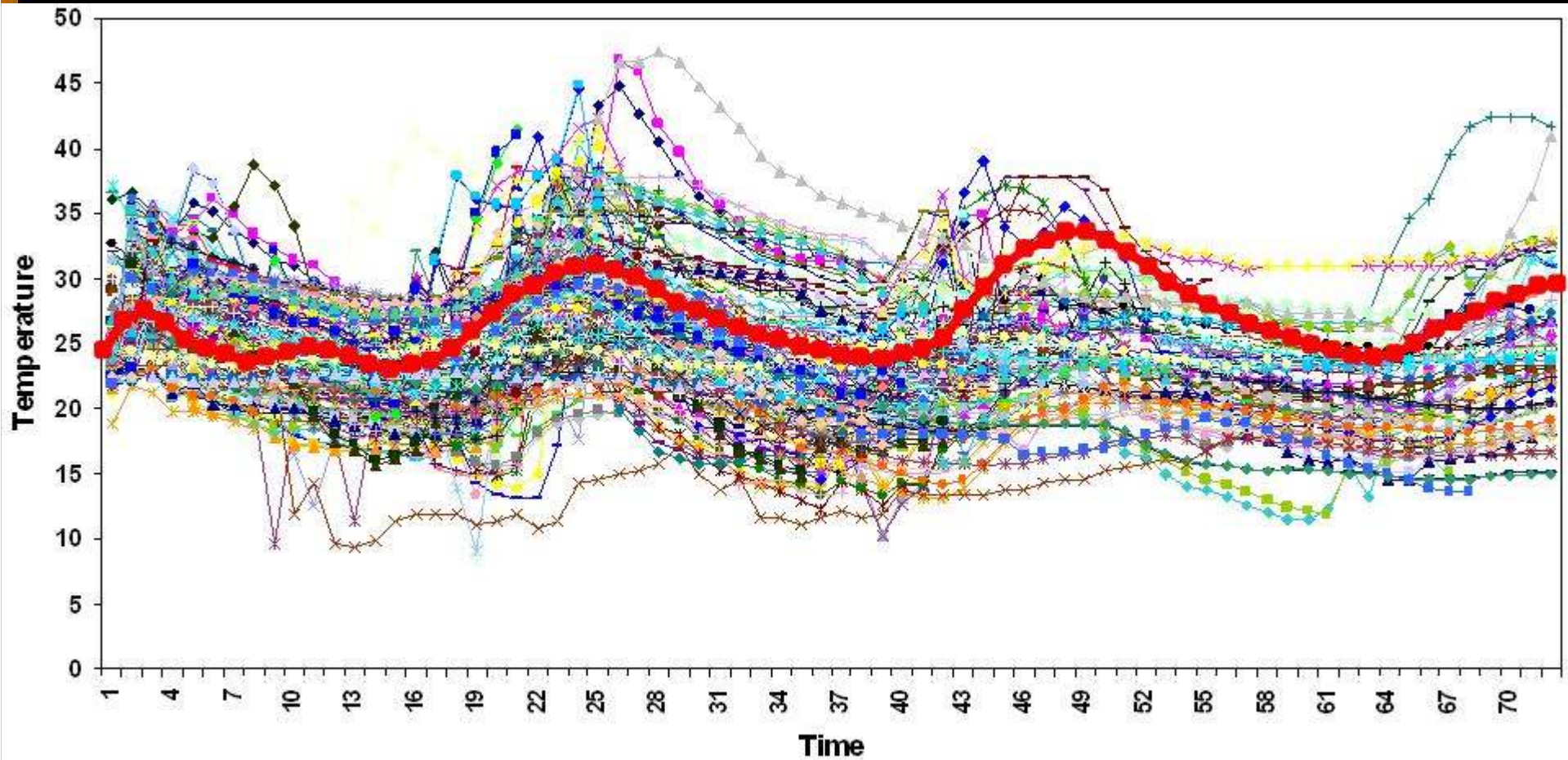
ISTA-016  
Report  
Jean-Pierre Emond



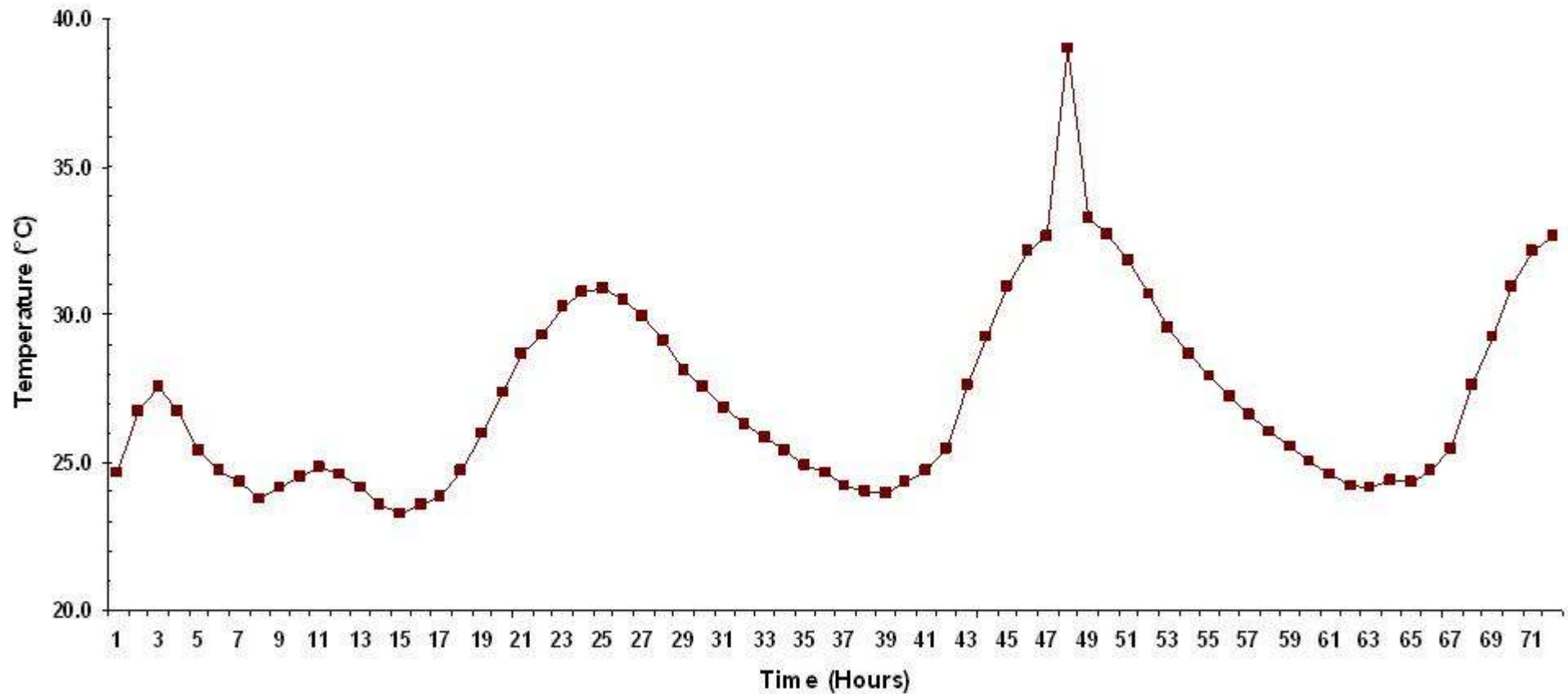
# Comparison of Color



# Raw Data / 99% Profile



# 72- Hours Heat Profile



# End Results of the Study

- New profiles developed
- ISTA will incorporate the new Hot and Cold Profiles in its Test Procedure 7D
  - Thermal Controlled Transport Packaging for Parcel Delivery System Shipments
- This is only the start of ISTA Test Standards for “Cold Chain”



# Thank You!

**Eric Joneson**

**[eric\\_joneson@lansmont.com](mailto:eric_joneson@lansmont.com)**