PREQUALIFICATION
THERMAL PERFORMANCE TESTS

KODIAKOOLER® Part #'s

27016K
27026K
27036K
27296K

Corporate Offices: 143 Barley Park Lane, Mooresville, NC 28115
866.779.4945
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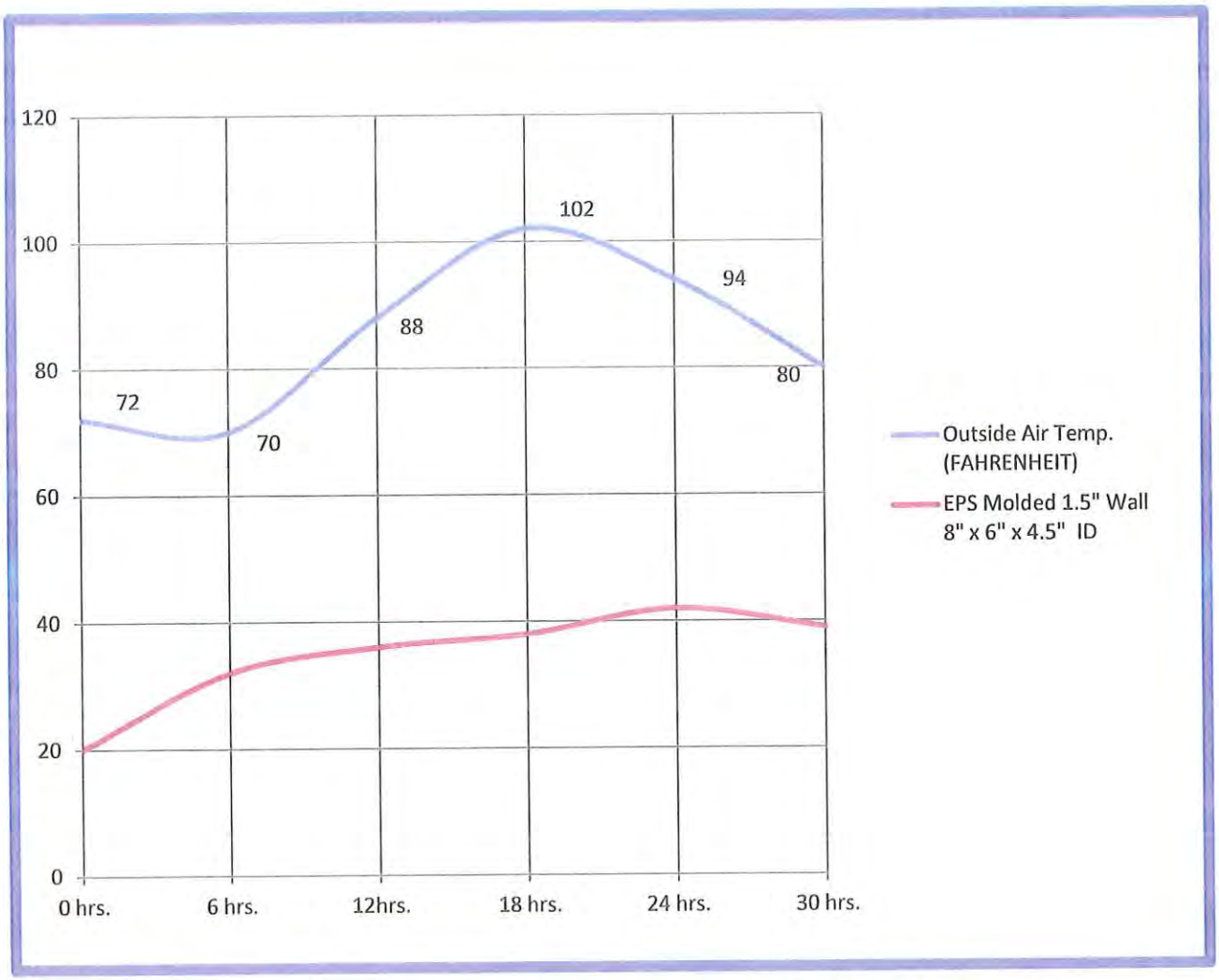
Providence Packaging
Prequalification Test
30 Hour Thermal Performance
27016K



Test was completed using 1.5" Wall EPS Molded Foam Cooler 8" x 6" x 4.5" and (1) 24 ounce gel pack
All void areas inside of packages were filled with 3/16" bubble-wrap
Outside Temperature profile is based on using ground transportation during a summer shipping cycle.

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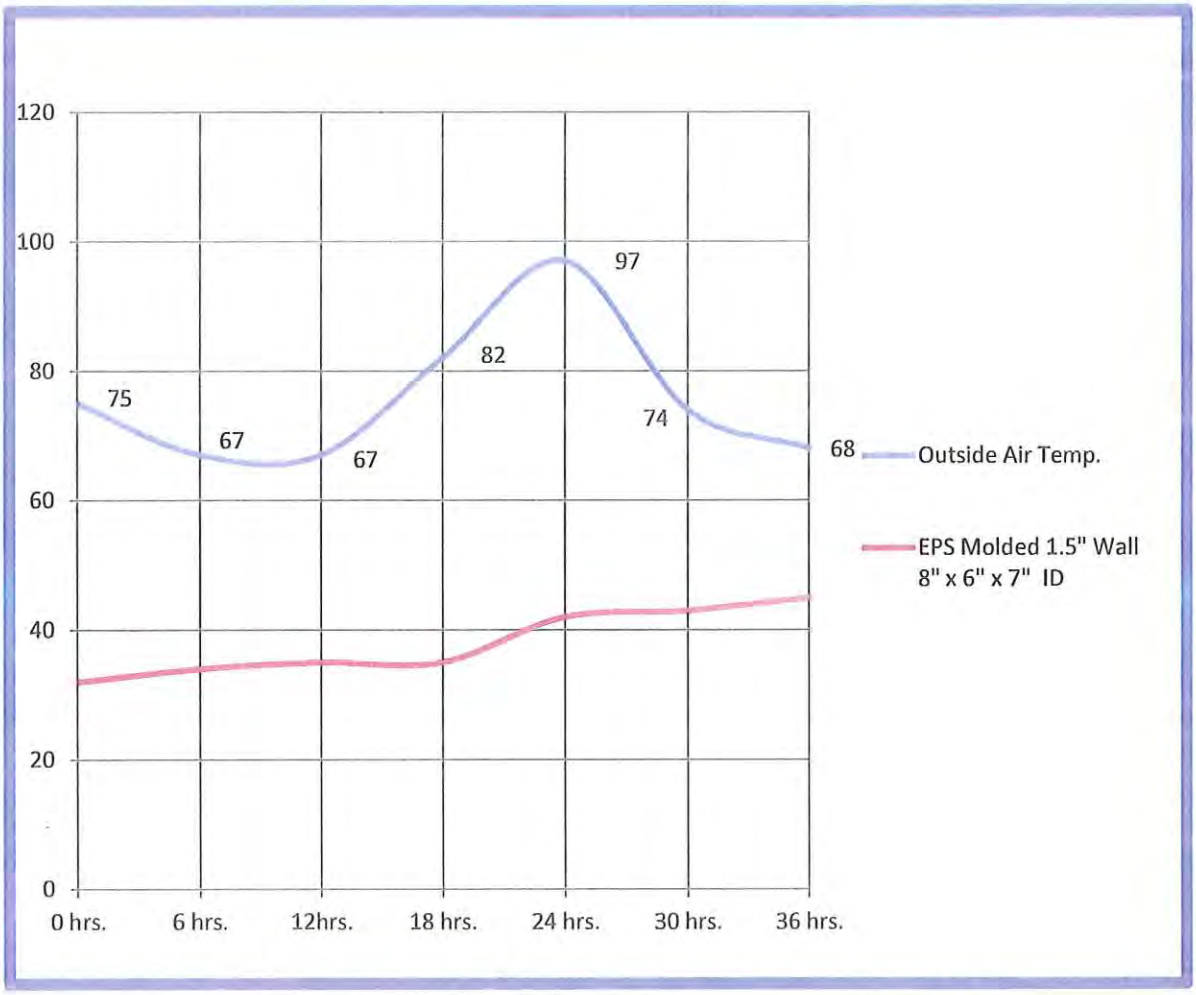
Providence Packaging
Prequalification Test
36 Hour Thermal Performance
27026K



Test was completed using 1.5" Wall EPS Molded Foam Cooler 8" x 6" x 7" and (2) 24 ounce bags of wet ice
All void areas inside of packages were filled with 3/16" bubble-wrap
Outside Temperature profile is based on using ground transportation during a summer shipping cycle.

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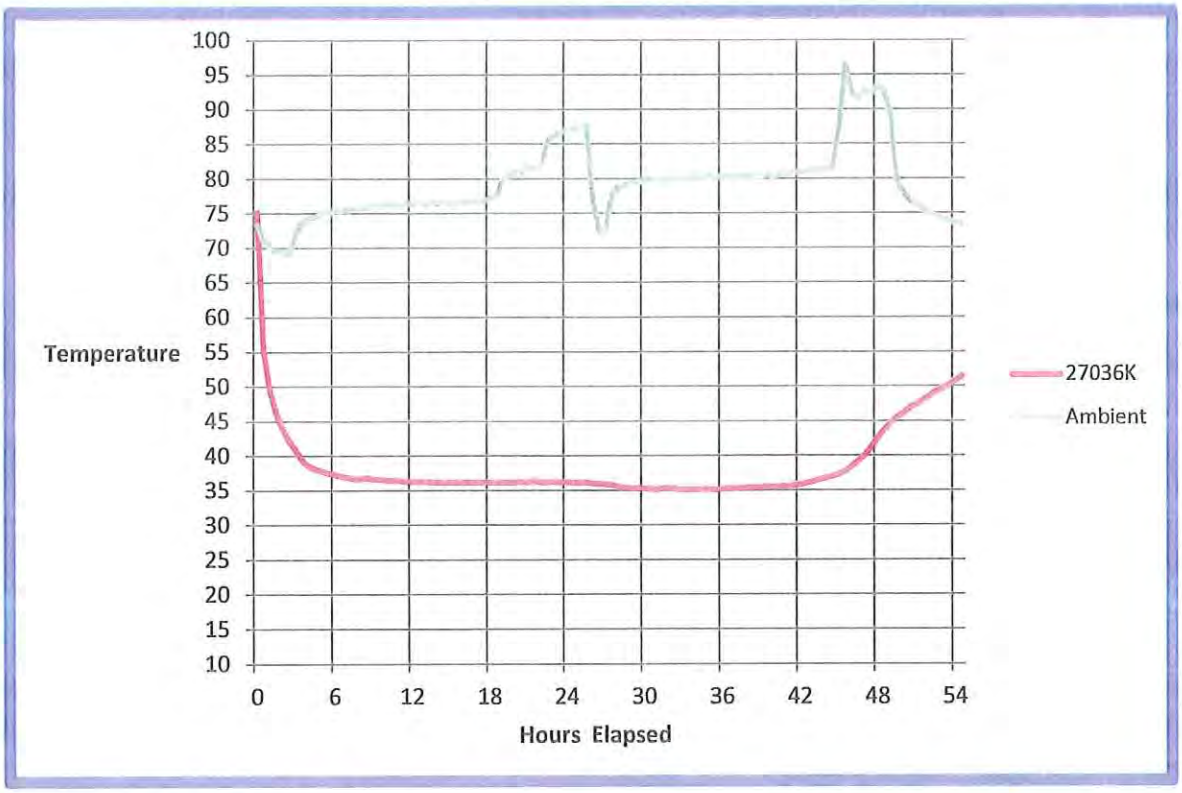
Providence Packaging
Prequalification Test
48 Hour Thermal Performance
27036K



Test was conducted using the 27036K cooler (8" x 6" x 9") and packed in the following manner:
Line cooler with 2 poly bags
Place one foam eye insert (PU6x4x2DCC) with tissue containers inside poly liners
Place two melting 24 oz wet ice blocks on either side of foam insert, Pour 8 oz of cold water on foam insert
Place a second foam insert perpendicular on top of first insert
Place two melting 24 oz wet ice blocks on top of the second foam insert
Fold over polybags. Place lid on cooler.

Outside Temperature profile is based on using ground transportation during a summer shipping cycle.

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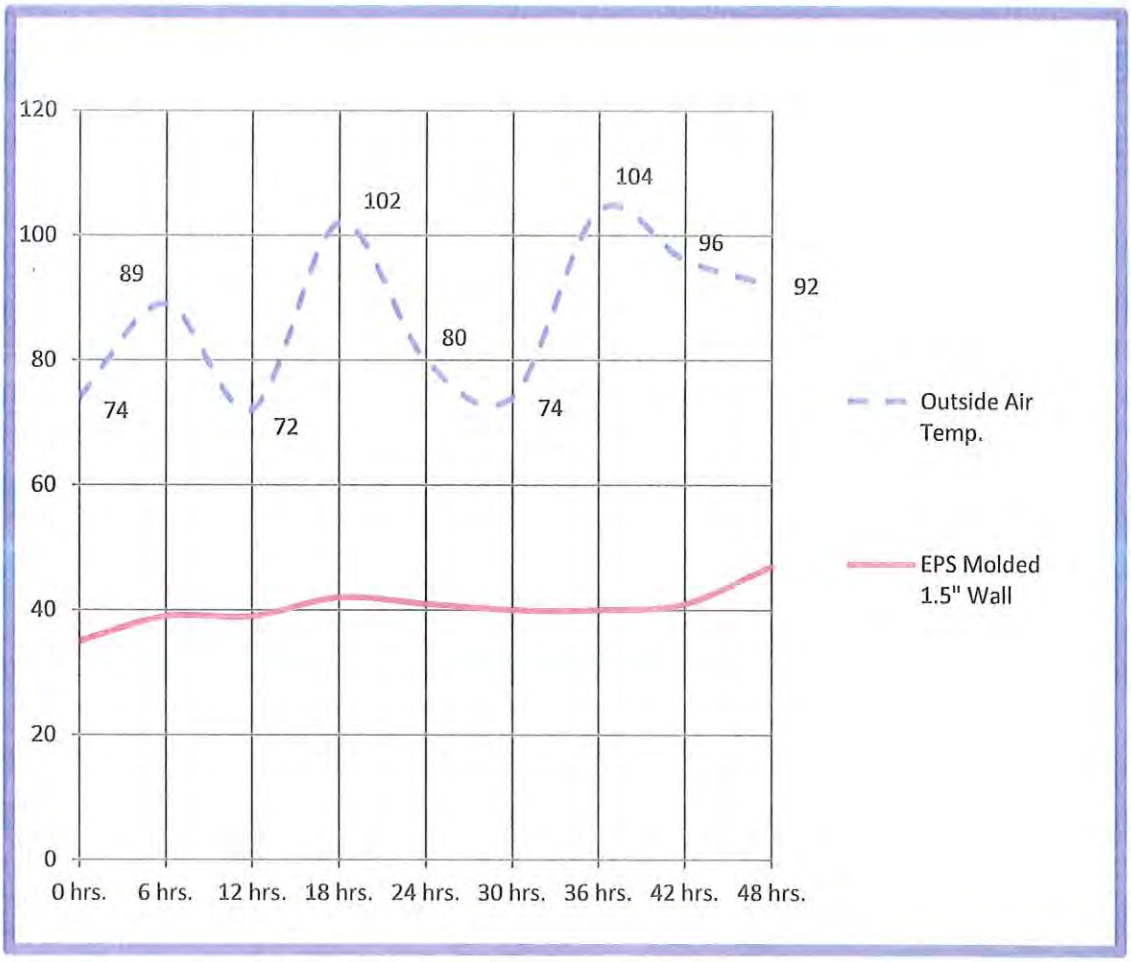
Providence Packaging
Prequalification Test
48 Hour Thermal Performance
27296K



Test was completed using 27296K COOLER (10.5" x 8" x 9.25") and packed using Cleveland Eye Bank protocol for international shippers with (20) 4.5" x 4.5" x 1.5" ice blocks inside.
Outside Temperature profile is based on using ground transportation during a summer shipping cycle.

www.ProvidencePackaging.com
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Summary of Final Report

Insulated Shipping Container Validation

PREPARED FOR

VISION SHARE

108 Acorn Hill Lane
Apex, NC 27502

PREPARED BY

Thomas D. Miller, BS
Director of Regulatory Affairs and Contracts, Vision Share

Andrew J. Maxwell, BA, CEBT
Quality Assurance Coordinator, SightLife

Thomas D. Lindquist, PhD, MD
Medical Director, SightLife

In the daily operation of eye banks, the transportation of corneas is an essential part of the supply chain. Current industry standards require that eye banks use a packaging method designed to prevent freezing of tissue and to maintain cool storage. The package content must demonstrate residual coolant in effect at the time of use, removal to mechanical storage or replacement of the coolant.

This validation study was designed to determine the interval of cooling effect of Insulated Shipping Containers in controlled and non-controlled shipping environments. This study shows that when optimal current practices and procedures are followed proper cooling requirements can be met. This applies for shipping corneal tissue locally, nationally, and internationally to surgeons and blood samples nationally to serology-testing laboratory.

The suitability of small, medium and large Insulated Shipping Containers and industry related packing procedures used by the eye banking industry in the United States were assessed. This report encompasses the results related to packing, shipping and monitoring of temperature data loggers during actual shipping events that simulated current practices utilized by industry for packing and shipping of corneal tissue. The containers were also tested against ISTA 5B/7D standards as shown in the BSTA extreme summer profile challenge.

Measuring internal temperature, amount of ice, and external temperature, allowed us to develop a predictive mathematical model. This modeling can greatly improve shipping practices by providing accurate information on expected internal temperatures at various external temperatures. This validation study model will help shippers make decisions on the proper package to ship corneas locally, nationally and internationally, helping to improve outcomes on corneal transplantation.

Small Insulated Shipping Containers are preferred for shipping corneas locally for times up to 24 hours. Medium Insulated Shipping Containers are preferred for shipping corneas and blood for serology testing locally, nationally and internationally for times up to 48 hours. Large shipping containers are preferred for shipping corneas internationally for up to 72 hours.

All sizes studied maintain proper cooling effect when the appropriate grams of wet ice are packaged for the needed time interval. Key considerations are temperature of shipping route, destination and quantity of wet ice packed. This assures that the amount of cooling effect over time will suffice.

Final Report

Insulated Shipping Container Validation

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Thomas D. Miller, BS
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Thomas D. Lindquist, PhD, MD
Medical Director, SightLife

DATE
04/05/10

PROPRIETARY INFORMATION

Shipping Container Validation Study

1.0 INTRODUCTION

1.1 In the daily operation of eye banks, the transportation of corneas is an essential part of the supply chain. Current industry standards require that eye banks use a packaging method designed to prevent freezing of tissue and to maintain cool storage. The package content must demonstrate residual coolant in effect at the time of use, removal to mechanical storage or replacement of the coolant. This validation study was designed to determine the interval of cooling effect of Insulated Shipping Containers in controlled and non-controlled shipping environments.

2.0 PURPOSE

2.1 Current Good Tissue Practice for Manufacturers of Human Cellular and Tissue-Based Products under 21 CFR 1271.195 requires establishments to identify any environmental conditions that require monitoring and *control*. This rule requires that procedures be written for environmental control and monitoring activities of systems where an environmental condition could have an adverse effect on the tissue-based product, causing contamination or cross-contamination.

2.2 Eye Bank Association of America Medical Standard L2.000 requires that an eye bank use a packaging method designed to maintain cool storage where the package content demonstrates remaining coolant effect at the time of use, removal to mechanical storage or replacement of the coolant. The package must also prevent freezing.

2.3 This validation study shows that when optimal current practices and procedures are followed proper cooling requirements can be met. This applies for shipping corneal tissue and blood samples to and from an eye bank and serology-testing laboratory, locally, nationally and internationally

2.4 This validation study was completed to determine the interval cooling effect of Insulated Shipping Containers in controlled and non-controlled shipping environments that included worse case temperature scenarios as shown on Appendix 18, 19 and 20.

3.0 SCOPE

3.1 The suitability of small, medium and large Insulated Shipping Containers and industry related packing procedures used by the eye banking industry in the United States were assessed.

3.2 This report encompasses the results related to packing, shipping and monitoring of temperature data loggers during actual shipping events that simulated current practices utilized by industry for packing and shipping of corneal tissue.

4.0 MATERIALS

4.1 Insulated Shipping Containers and inserts:

a. *Shipping Container Dimensions*

b. The average size of shipping boxes tested featured a thick-walled container of 1.5", expanded polystyrene foam. A tight fitting lid plug which assures thermal efficiency.

c. SMALL – inside length 8", inside width 6", inside depth 4.25"

d. MEDIUM - inside length 8", inside width 6", inside depth 9.75"

e. LARGE - inside length 11", inside width 8.5", inside depth 9.25"

f. Outer cases are 200-lb. test corrugated cardboard

g. Generic shipping boxes similar to the type used in this validation study should return similar results when utilized. Using smaller or larger containers than those identified in this validation study may decrease or increase thermal shipping times.

4.2 Dickson SK500 Temperature Data Loggers:

a. Temperature Accuracy ±1.8F (±1C) over range -4 to +158°F (-20 to +70°C)

b. Temperature Range -4 to 158F, -20 to 70C

c. Calibration - is the process of making a zero (low scale) adjustment so that it matches exactly to a known standard, and a separate span (high scale) adjustment that also matches the unit exactly to a known standard. These two independent adjustment procedures are repeated until the unit matches the known standard, within its allowed specification. After this process is complete, the unit is accurate throughout its full measurement range.

d. Approval – CE approved

e. Data Logger Calibration – the data loggers were calibrated in June 2008.

4.3 Foam inserts

4.4 Plastic bag(s)

a. For the foam insert

b. Dickson SK500 data logger (4" x 7" zip lock)

c. For wet ice (12" x 18")

4.5 Packing Tape

4.6 Ice bag sealer is an American International Electronics Impulse Sealer with Magnet Model AIE-405MC

4.7 Ice Scoop is a 24 oz - 710 ml

4.8 Scale - Francotyp-Postalia P150 with a weight capacity of 0.2 oz. to 150 lb. and accuracy of +/- 0.2 oz. from 0-4 lb. and +/- 0.5 oz. from 4-150 lb.

4.9 Wet ice from a Manitowoc model QM-45, self contained air cooled dice cube ice maker

5.0 PACKING AND SHIPPING POLICIES AND PROCEDURES

5.1 Vision Share Facilities are located across various regions/climates nationwide.

5.2 Generic packing and shipping procedures utilized for this validation study should return similar results when closely followed.

5.3 The procedure used in this validation study are described in L2.000 Packaging, Sealing and Packing for Transport in the Procedures Manual of the Eye Bank Association of America.

6.0 SAMPLING SCHEME

6.1 This report includes a control set of data, a data set for winter months (October – March) and a data set summer months (April – September) as well as an extreme temperature challenge.

6.2 The sampling frequency consisted of at least 10 sampling events in a warm climate, 10 sampling events in a cold climate and 10 sampling events in a controlled ambient environment during winter months (October – March) and summer months (April – September).

6.3 A sampling event consisted of packing, shipping and storage of the data logger in the shipping container packed with various quantities of wet ice, stored for different times, and differing temperatures.

6.4 Sampling events were followed during actual shipping events, measuring time and temperature of the shipping box's internal and external (ambient) temperature.

7.0 METHODS

7.1 Summary:

The Insulated Shipping Containers in this validation study were packed following industry practices with wet ice quantities that varied from 3500-4800 grams depending on the size of shipping container. Commercially available temperature monitors were packaged as would a cornea-viewing chamber or vial be packed for shipping. The packages were subjected to controlled environments (regulated office), non-controlled environments (i.e. couriers, airlines, FedEx to different climates), and an elevated summer conditions with an environmental chamber test.

The control group was given limited exposure to temperature variation in order to establish a base line cooling effect at warm temperature (assuming no external cooling). The shippers were continuously monitored internally and externally using data loggers recording data (time & temperature) every 2 minutes. The data was evaluated to determine time interval where the terminal cooling effect remained at or below 8°C. The time interval to weight of ice was used to determine cooling effect of the box.

The non-controlled (field trials) group was exposed to various external temperatures, experienced by actual conditions encountered during transport. Due to significant regional temperature differences, we identified differing warm and cold climates in the United States and shipped packages to these regions. The data was collected the same for both regions. Depicted are graphs for controlled and non-controlled shipping events.

Additionally, an environmental chamber test was used to simulate a 72 hour elevated summer conditions (Extreme Summer Profile) per BSTA requirements. The shippers were monitored internally and externally using data loggers recording data (time & temperature) every 2 minutes. The data was evaluated to determine time interval where the terminal cooling effect remained at or below 8°C. Four (4) identical packages were placed into the environmental chamber where the temperature was recorded every 10 minutes for the duration of the test. Depicted are graphs for the environmental chamber test.

7.2 Data Logger:

a. Using Dickson software, program the data logger to:

   1. Set data logger to record temperature at no less than 1 minute and no longer than every 5 minutes
   2. Record without looping (writing over previous data when full)
   3. Set appropriate date and time
   4. Set measurement to Celsius

b. Reset the data logger

c. Place the logger in a foam block

d. Seal the data logger and foam block in a plastic bag

e. Place data logger in tissue refrigerator to pre-cool prior to packing (for a minimum of 30 minutes)

7.3 Shipment:

a. *Small, Medium or Large Shipping Container*

b. Inspect shipping container, ensuring it is labeled in accordance with industry standards.

   1. Seal data logger in a plastic bag.

      i. Sealed plastic bag is used to prevent possible damage of data logger by moisture.

b. Place foam block with sealed data logger into a polystyrene box.

1. Foam block prevents excessive movement within the polystyrene box.

c. Place one layer of paper towels over top of the foam block to insulate the data logger from direct contact with the wet ice and to absorb any condensation or leakage that may occur.

d. Place wet ice sealed in plastic bag(s) into Large and Medium shipping containers.

1. Ensure enough wet ice is used to fill shipping container.
2. Wet ice is ice at its melting point. If ice is below its melting point, add water to begin melting process.
3. Measure individual bags of ice and record a total weight of wet ice used.

e. Place the lid on the Styrofoam box and secure with packing tape.

1. Seal around lid of polystyrene box according to airline regulations and put in a box shell.
2. A secured box provides a waterproof container and preserves coolness

f. Use a box shell, seal lid and all edges with packing tape.

1. Secures box against potential tampering and further prevents possible leakage of fluids.

g. Place proper handling labels on the outside of the shipping container indicating safe shipping and storage methods.

1. Handling labels clearly identify the statement "DO NOT FREEZE" to prevent mistakes in transit and to keep the shipping box from freezing.

6.2 Environmental chamber test

a. All protocols followed for shipment as described above

b. 4 boxes were placed in chamber and subjected to temperatures as follows:

1. 22°C for 5 hours
2. 30°C for 5 hours
3. 22°C for 5 hours
4. 20°C for 5 hours
5. 25°C for 5 hours
6. 35°C for 5 hours
7. 25°C for 5 hours
8. 30°C for 5 hours
9. 22°C for 5 hours
10. 25°C for 5 hours
11. 22°C for 5 hours
12. 30°C for 5 hours
13. 22°C for 5 hours
14. 20°C for 5 hours
15. 25°C for 4 hours

6.3 Measurements

a. Wet ice was measured by weight prior to packing using a calibrated scale.

b. Data logger(s) performed interval temperature measurements.

c. Time was recorded with temperature via data logger(s).

7.0 PROTOCOL CHANGES

7.1 The following protocol changes, revisions and reasons for the change are documented in this section, and will remain part of the permanent file for this validation study.

7.2 The Researcher was notified concerning changes, and revisions as the event occurred, none have an effect on the validity of this validation study.

8.0 DATA RETENTION

8.1 A copy of this report will be kept on file at the Vision Share corporate office for 10 years from the date of validation study completion.

9.0 DATA COLLECTION AND EVALUATION

9.1 Data collected is summarized and shown on computer-generated charts.

9.2 The loggers recorded the time intervals from the start of packaging until temperature readings from the loggers were consistently above 8°C.

9.3 Correlation of time intervals from start to above 8°C.

a. Graph the volume of ice to time

b. Determine the linear regression

c. Use the equation of the line to determine correlation of ice quantity to time of refrigeration at or below 8°C.

10.0 STATISTICAL ANALYSIS

10.1 Statistical analysis was performed on the collected data points as shown on Appendix 1, 2 and 3.

10.2 The controlled shipping group consisted of 16 recorded events with an external temperature average of 21.8°C and a range of 7°C. Ice quantity variation per shipping box had a mean 4438.5 grams, mode of 4310 grams, and range of 740 grams. The ice from all the controlled events totaled 71016.6 grams of wet ice and produced 82231.0 minutes of cooling effect at or below 8°C as shown on Appendix 3 – 13.

10.3 The total minutes of cooling effect at or below 8°C in the controlled shipping group gives a mean of 1.2 minutes per gram of wet ice as shown on Appendix 3.

10.4 The control group produced a result of grams of ice to time recorded to maintain a temperature at/or below 8°C resulting in a linear regression equation of y=0.5892x+1410.3. (y is grams of ice, x is minutes) as shown on Appendix 2, Table 1.

10.5 The non-controlled (field trials) shipping group consisted of 15 recorded events with an external temperature average of 15.1°C, and a range of 20.5°C. Ice quantity variation per shipping box had a mean 4017.1 grams, mode of 4167.4 grams, and range of 1525.2 grams. The ice from all non-controlled events totaled at 56239.7 grams of wet ice produced 104177.0 minutes of cooling effect at or below 8°C as shown on Appendix 14, 15, 16 and 17.

10.6 The non-controlled (field trials) shipping group minutes of cooling effect at or below 8°C gives a mean of 1.9 minutes per gram of wet ice as shown on Appendix 3.

10.7 The non-controlled (field trials) group produced a result of grams of ice to time recorded to maintain a temperature at/or below 8°C resulting in a linear regression equation of y=0.5388x+8.0263. (y is grams of ice, x is minutes) as shown on Appendix 18 and 19.

10.8 The Extreme Summer Profile challenge group consisted of four recorded events with the medium and four recorded events with the large shipping containers with varying external temperatures known as an extreme summer profile as shown on Appendix 2, Table 2.

10.9 The challenge group average quantity of ice in each medium shipping container was 1912.95 grams producing a cooling effect of between 49.5 to 65 hours with an average of 57.5 hours as shown on Appendix 18.

10.10 The challenge group average quantity of ice in each large shipping container was 4273.80 grams producing a cooling effect of between 77.25 to 83.5 hours with an average of 81 hours as shown on Appendix 19.

10.11 The challenge group minutes of cooling effect at or below 8°C gives a mean of 1.8 minutes per gram of wet ice for the medium and 1.15 minutes per gram of wet ice for the large shipping container as shown on Appendix 19.

10.12 The Insulated Shipping Containers provided an overall range of cooling effect at or less than 8°C for an average of 1.2 and 1.85 minutes per gram of wet ice with external temperatures ranges from 21.8°C to 15.1°C respectively as shown on Appendix 3.

10.13 With 4500 grams of packaged wet ice and an average ambient temperature of 15.1°C, the cooling effect lasted 138.9 hours. With 4500 grams of packaged wet ice and an average ambient temperature of 21.8°C, the cooling effect lasted 87.4 hours. This is consistent with what was seen with the Extreme Summer Profile as shown on Appendix 18 and 19.

11.0 SUMMARY / CONCLUSIONS

11.1 Small, Medium and Large Insulated Shipping Containers were tested in controlled and non-controlled environments during summer and winter months. Also, they successfully passed BSTA Extreme Summer Profile challenges, which are part of the ISTA 5B /7D testing requirements as shown on Appendix 20.

11.2 Insulated Shipping Containers similar to those studied have proven reliable in maintaining the recommended storage and shipping temperatures for corneas intended for surgery as required by EBAA Medical Standard L2.000 Packaging, Sealing and Packing for Transport for many years.

11.3 Measuring internal temperature, amount of ice, and external temperature, allowed us to develop a predictive mathematical model. This modeling can greatly improve shipping practices by providing accurate information on expected internal temperatures at various external temperatures. A list of shipping destinations and recommended shipping container are shown on Appendix 21.

11.4 This validation study model will help shippers make decisions on the proper package to ship corneas locally, nationally and internationally, helping to improve outcomes on corneal transplantation. The equations utilized in this validation study do not work outside of the ranges used in this validation study.

11.5 This validation study did not evaluate ice blocks or gel packs for providing cooling effect.

11.6 Small Insulated Shipping Containers are preferred for shipping corneas locally and nationally during summer months for times up to 24 hours.

11.7 Medium Insulated Shipping Containers are preferred for shipping corneas and blood for serology testing locally, nationally and internationally during summer months for times up to 48 hours.

11.8 Large shipping containers are preferred for shipping corneas internationally during summer months up to 72 hours.

11.9 All sizes studied maintain proper cooling effect when the appropriate grams of wet ice are packaged for the needed time interval.

11.10 Key considerations are temperature of shipping route, destination and quantity of wet ice packed. This assures that the amount of cooling effect over time will suffice.

12.0 REGULATORY STATEMENT

12.1 The validation study referenced in this protocol was conducted in compliance with Current Good Tissue Practice for Manufacturer's of Human Cellular and Tissue-Based Products (21CFR1271.195).

13.0 REFERENCES

13.1 The ISTA Resource Book, International Safe Transit Association, 2006

13.2 ISTA 5B Focused Simulation for Thermal Performance Testing of Temperature Controlled Transport Packaging, 2002

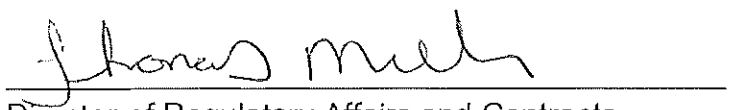
13.3 ISTA 7D Thermal Controlled Transport Packaging Parcel Delivery System Shipment, 2006

13.4 Food and Drug Administration's 21 CFR 1271.195 Good Tissue Practice Regulations

13.5 Food and Drug Administration's 21CFR 600.15 Biological Products, Temperatures during shipment

13.6 EBAA Medical Standards (November 2008) L2.000 Packaging, Sealing and Packing for Transport

14.0 REPORT APPROVAL



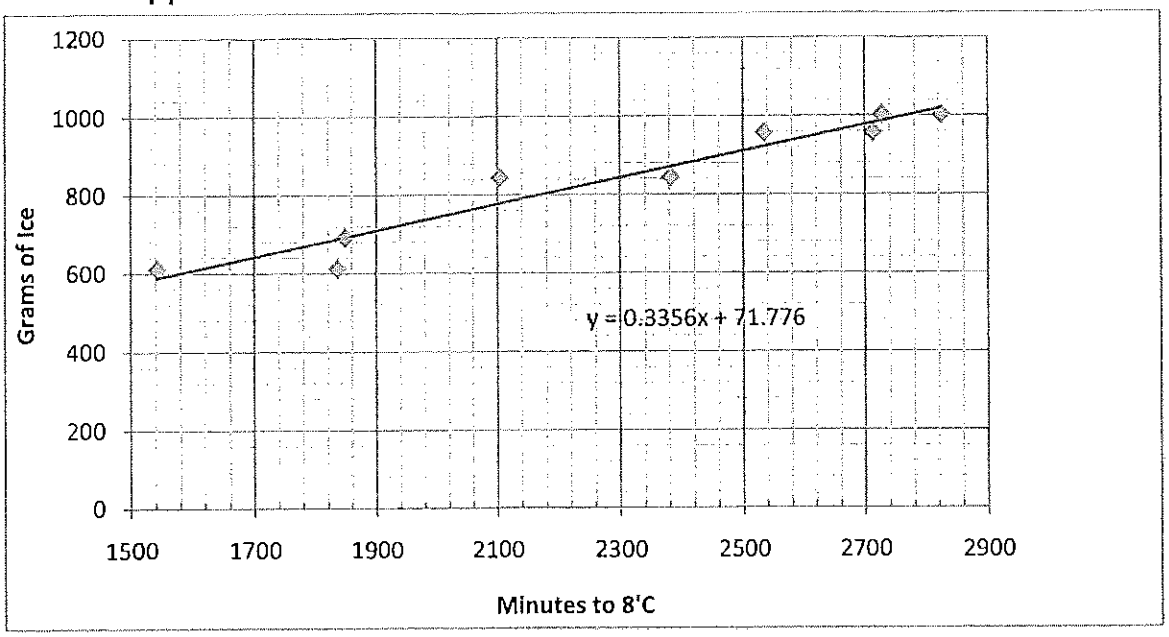
Director of Regulatory Affairs and Contracts

4/5/10

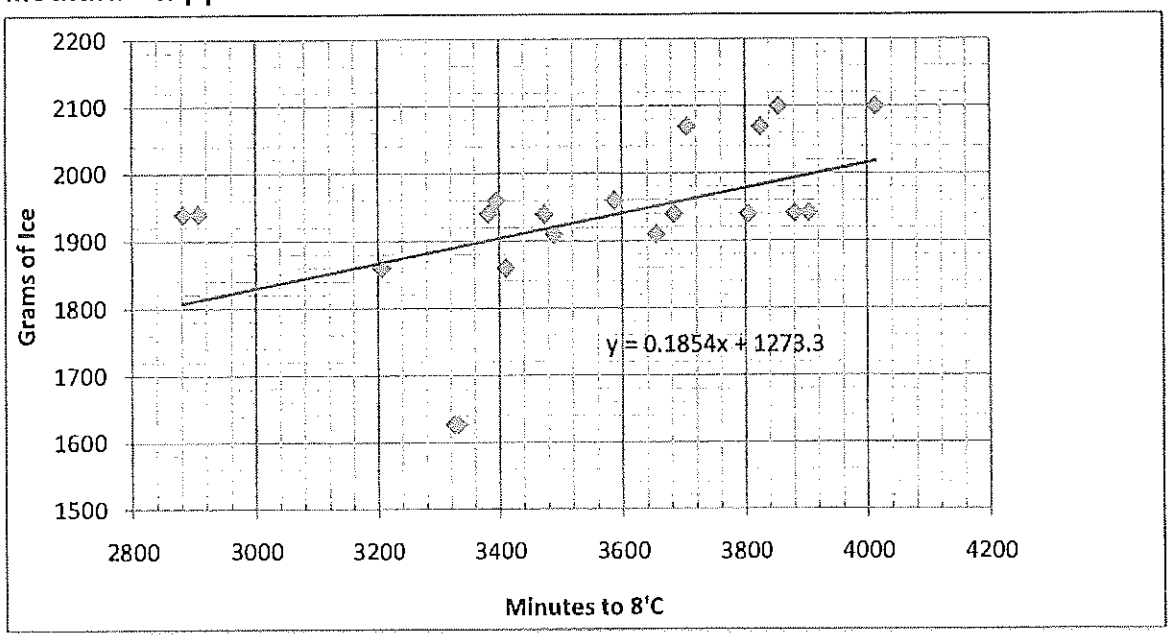
Date

Appendix 1

Small Shipper Minutes/Grams of Ice

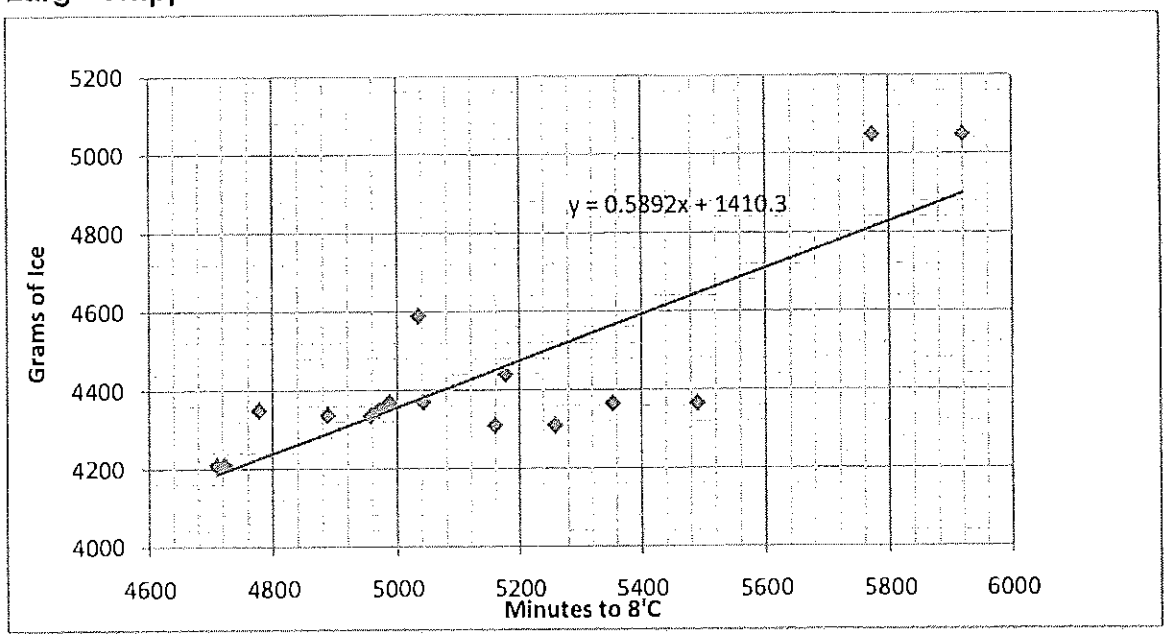


Medium Shipper Minutes/Grams of Ice

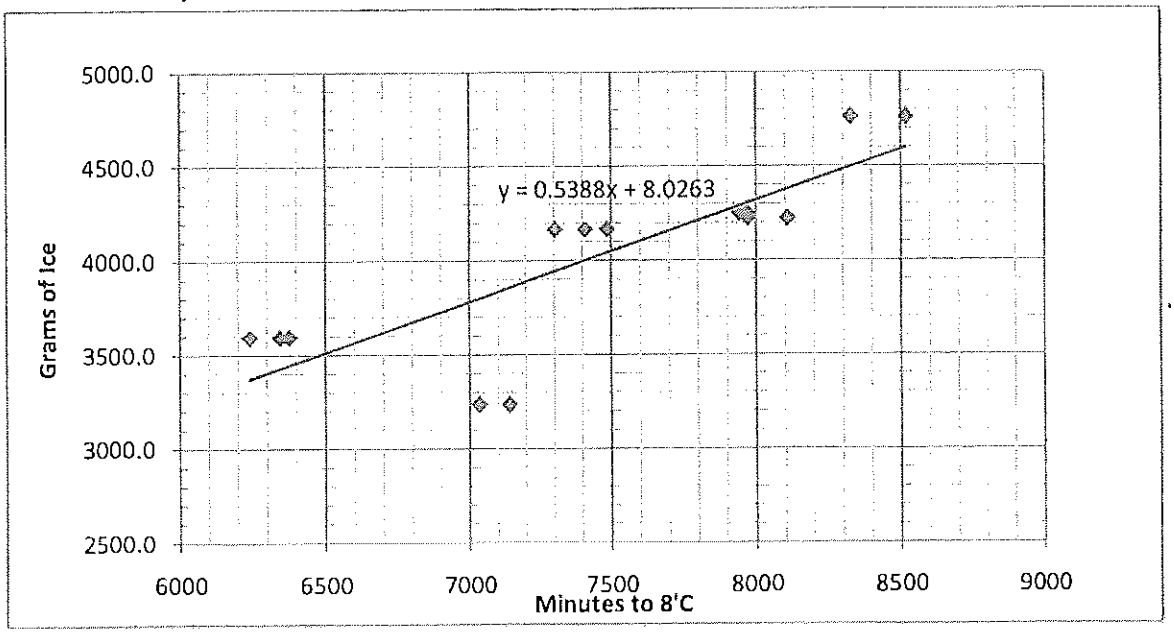


Appendix 2

Large Shipper Minutes/Grams of Ice



Control Graph Minutes/Grams of Ice

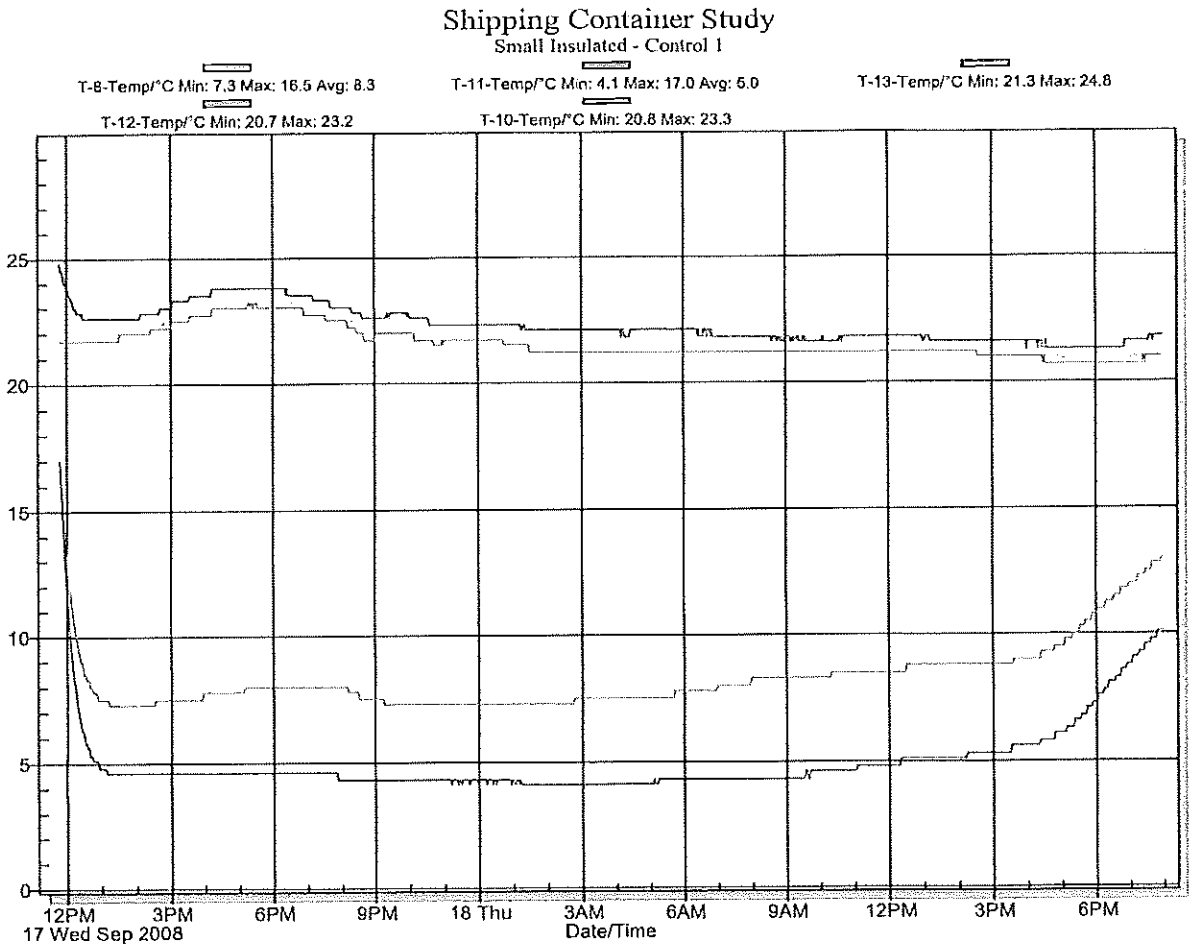


Appendix 3

Control and Field Trial Results

Range	Control Trials	Field Trials
Average Temperature (°C)	21.8	15.1
Minimum Temperature (°C)	18.7	4.2
Maximum Temperature (°C)	25.1	26.1
Average minutes/grams of ice	1.2	1.9
Regression of minutes/grams of ice	y=0.5892x + 1410.3	y=0.5388x + 8.0263

Appendix 4


Shipping Container Study
Small Insulated - Control 1
T-8-Temp/°C Min: 7.3 Max: 16.5 Avg: 8.3
T-11-Temp/°C Min: 4.1 Max: 17.0 Avg: 6.0
T-13-Temp/°C Min: 21.3 Max: 24.8
T-12-Temp/°C Min: 20.7 Max: 23.2
T-10-Temp/°C Min: 20.8 Max: 23.3
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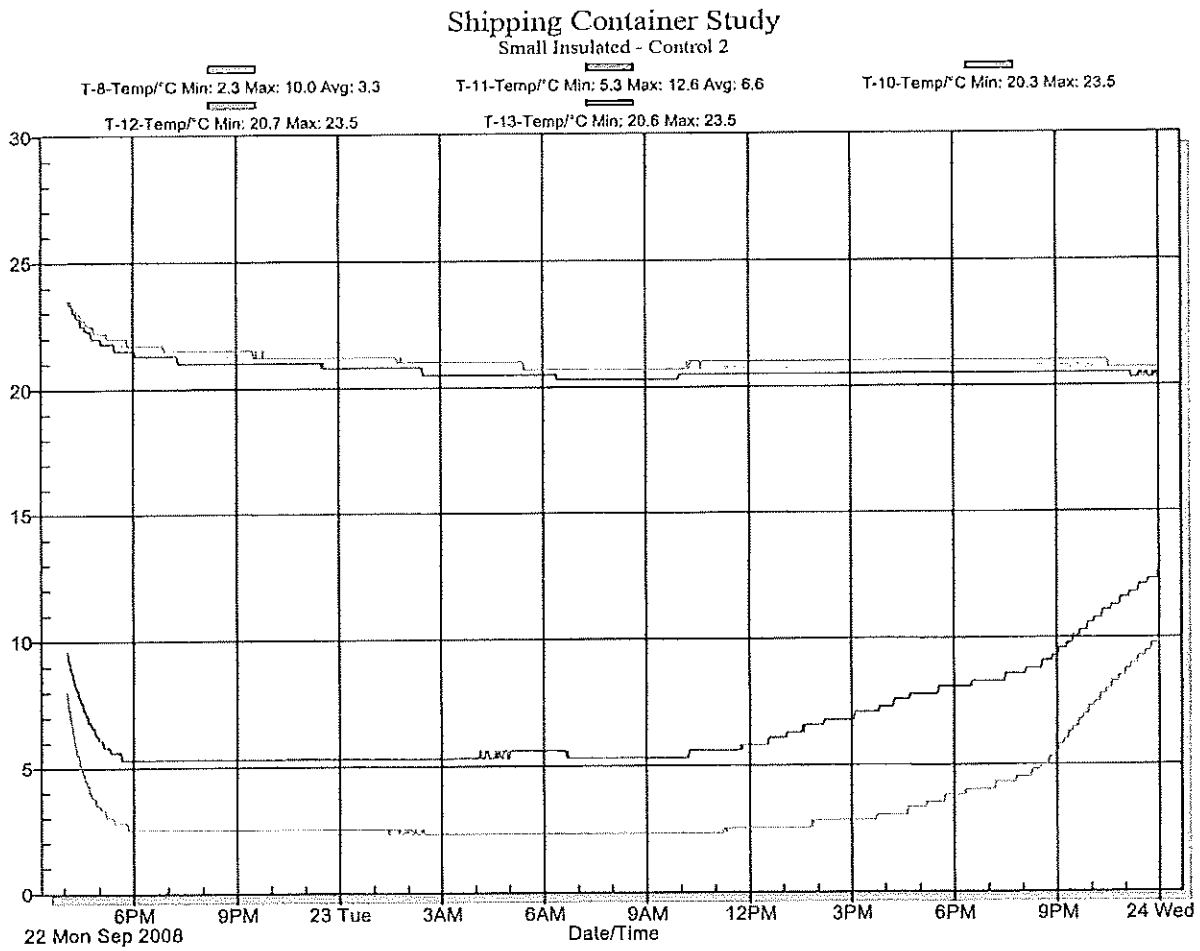
Appendix 5


Shipping Container Study
Small Insulated - Control 2
T-8-Temp/°C Min: 2.3 Max: 10.0 Avg: 3.3
T-11-Temp/°C Min: 5.3 Max: 12.6 Avg: 6.6
T-10-Temp/°C Min: 20.3 Max: 23.5
T-12-Temp/°C Min: 20.7 Max: 23.5
T-13-Temp/°C Min: 20.6 Max: 23.5
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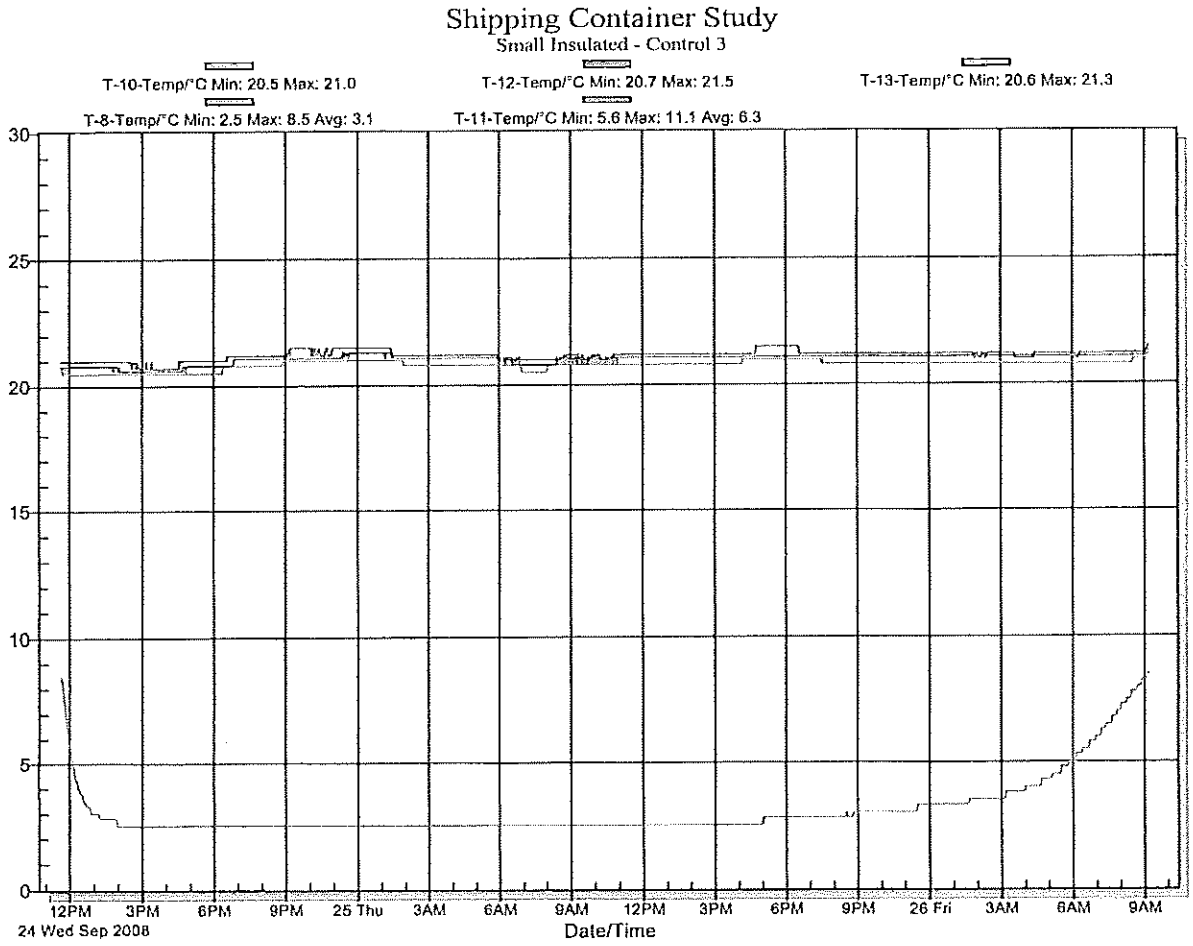
Appendix 6


Shipping Container Study
Small Insulated - Control 3
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T-12-Temp/°C Min: 20.7 Max: 21.5
T-13-Temp/°C Min: 20.6 Max: 21.3
T-8-Temp/°C Min: 2.5 Max: 8.5 Avg: 3.1
T-11-Temp/°C Min: 5.6 Max: 11.1 Avg: 6.3
30
25
20
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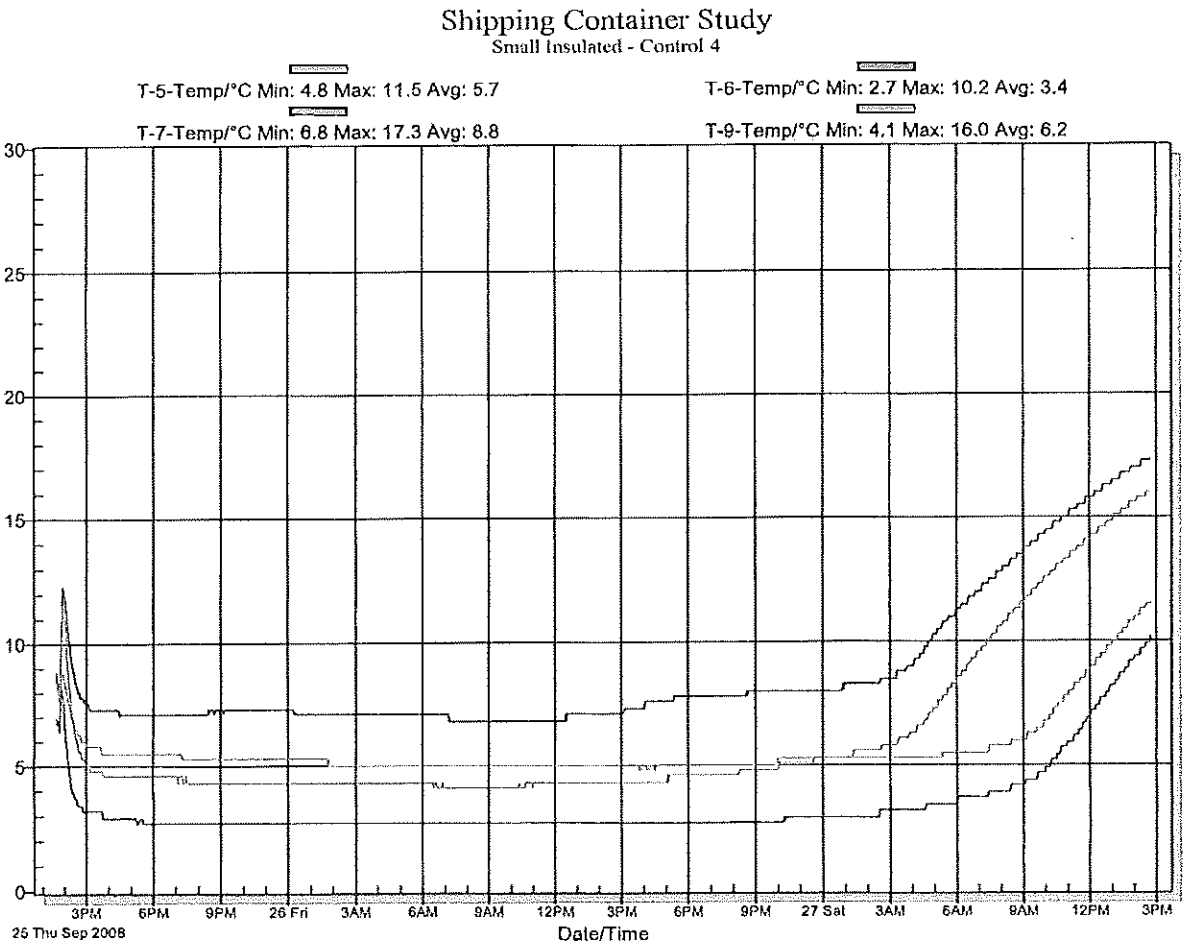
Appendix 7


Shipping Container Study
Small Insulated - Control 4
T-5-Temp/°C Min: 4.8 Max: 11.5 Avg: 5.7
T-6-Temp/°C Min: 2.7 Max: 10.2 Avg: 3.4
T-7-Temp/°C Min: 6.8 Max: 17.3 Avg: 8.8
T-9-Temp/°C Min: 4.1 Max: 16.0 Avg: 6.2
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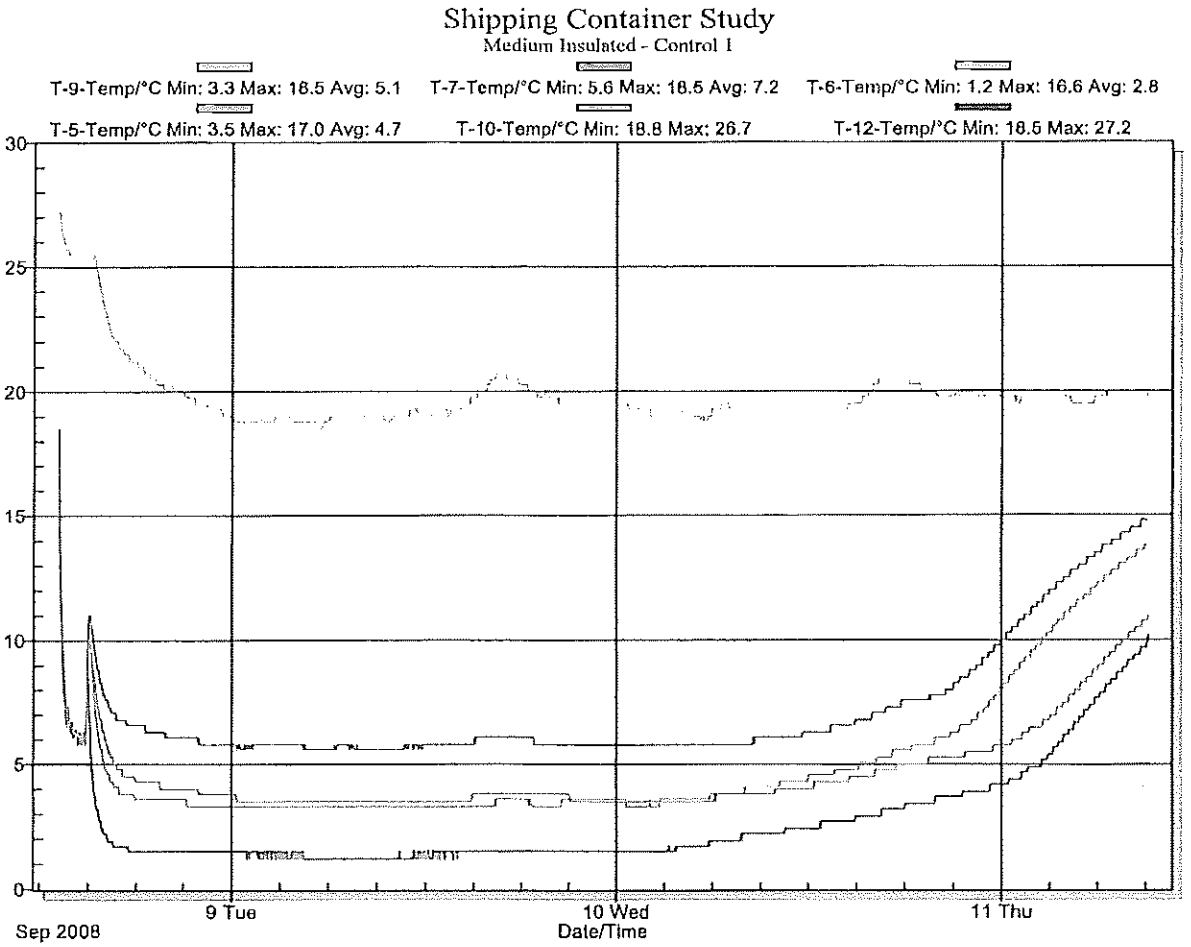
27 Sat
3AM
6AM
9AM
12PM
3PM
25 Thu Sep 2008
Date/Time

Appendix 8


Shipping Container Study
Medium Insulated - Control 1
T-9-Temp/°C Min: 3.3 Max: 18.5 Avg: 5.1
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T-6-Temp/°C Min: 1.2 Max: 16.6 Avg: 2.8
T-5-Temp/°C Min: 3.5 Max: 17.0 Avg: 4.7
T-10-Temp/°C Min: 18.8 Max: 26.7
T-12-Temp/°C Min: 18.5 Max: 27.2
30
25
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15
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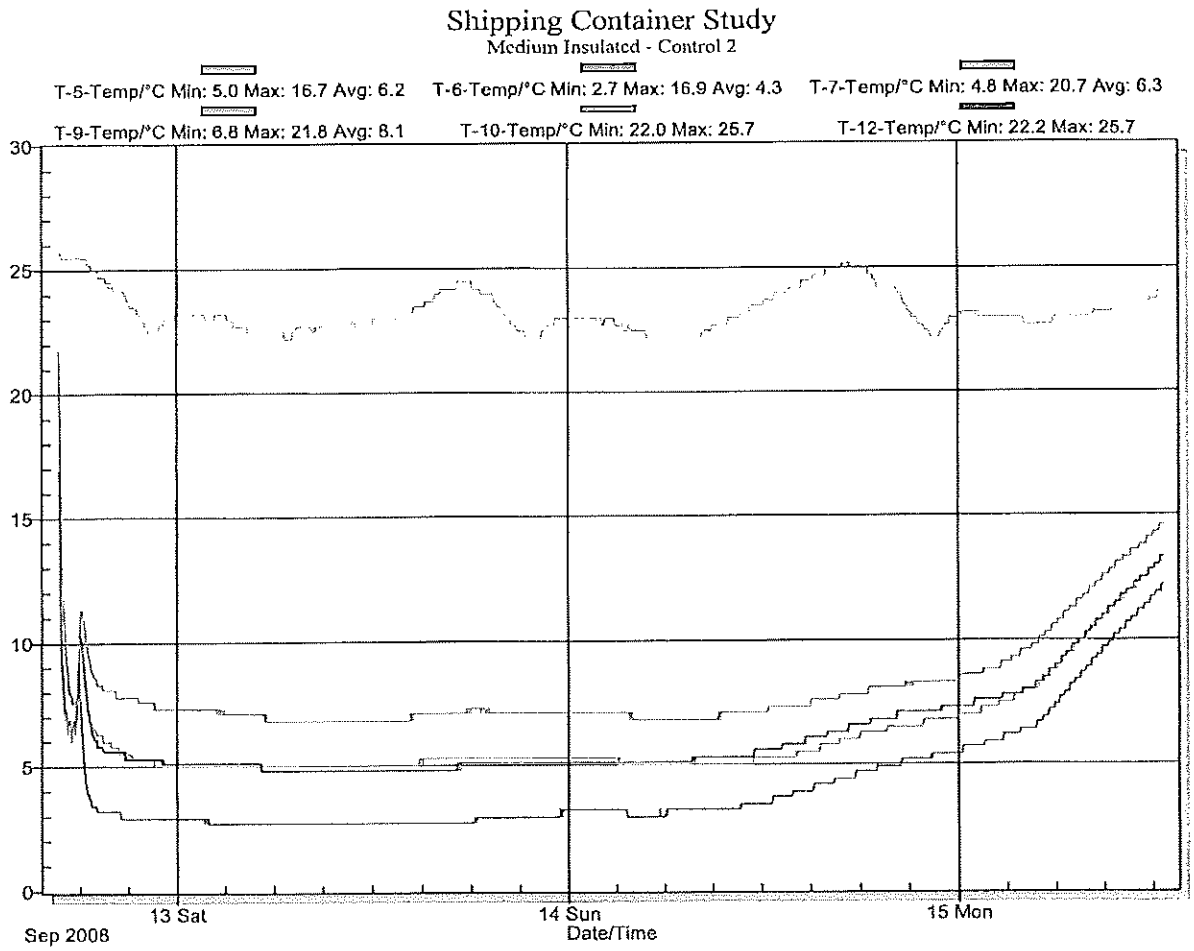
11 Thu
Sep 2008
Date/Time

Appendix 9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T-6-Temp/°C Min: 2.7 Max: 16.9 Avg: 4.3
T-7-Temp/°C Min: 4.8 Max: 20.7 Avg: 6.3
T-9-Temp/°C Min: 6.8 Max: 21.8 Avg: 8.1
T-10-Temp/°C Min: 22.0 Max: 25.7
T-12-Temp/°C Min: 22.2 Max: 25.7
30
25
20
15
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5
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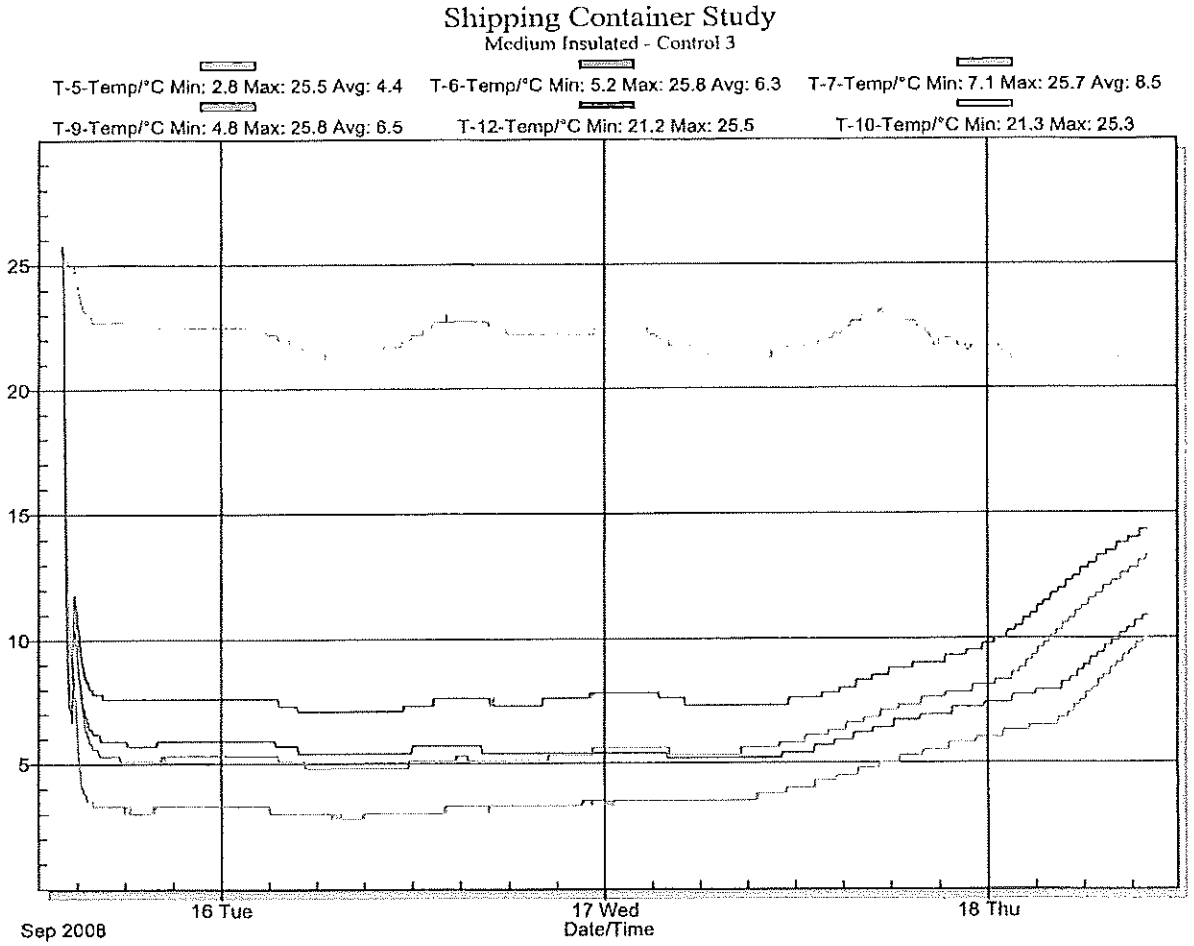
13 Sat
Sep 2008
14 Sun
15 Mon
Date/Time

Appendix 10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T-6-Temp/°C Min: 5.2 Max: 25.8 Avg: 6.3
T-7-Temp/°C Min: 7.1 Max: 25.7 Avg: 8.5
T-9-Temp/°C Min: 4.8 Max: 25.8 Avg: 6.5
T-12-Temp/°C Min: 21.2 Max: 25.5
T-10-Temp/°C Min: 21.3 Max: 25.3
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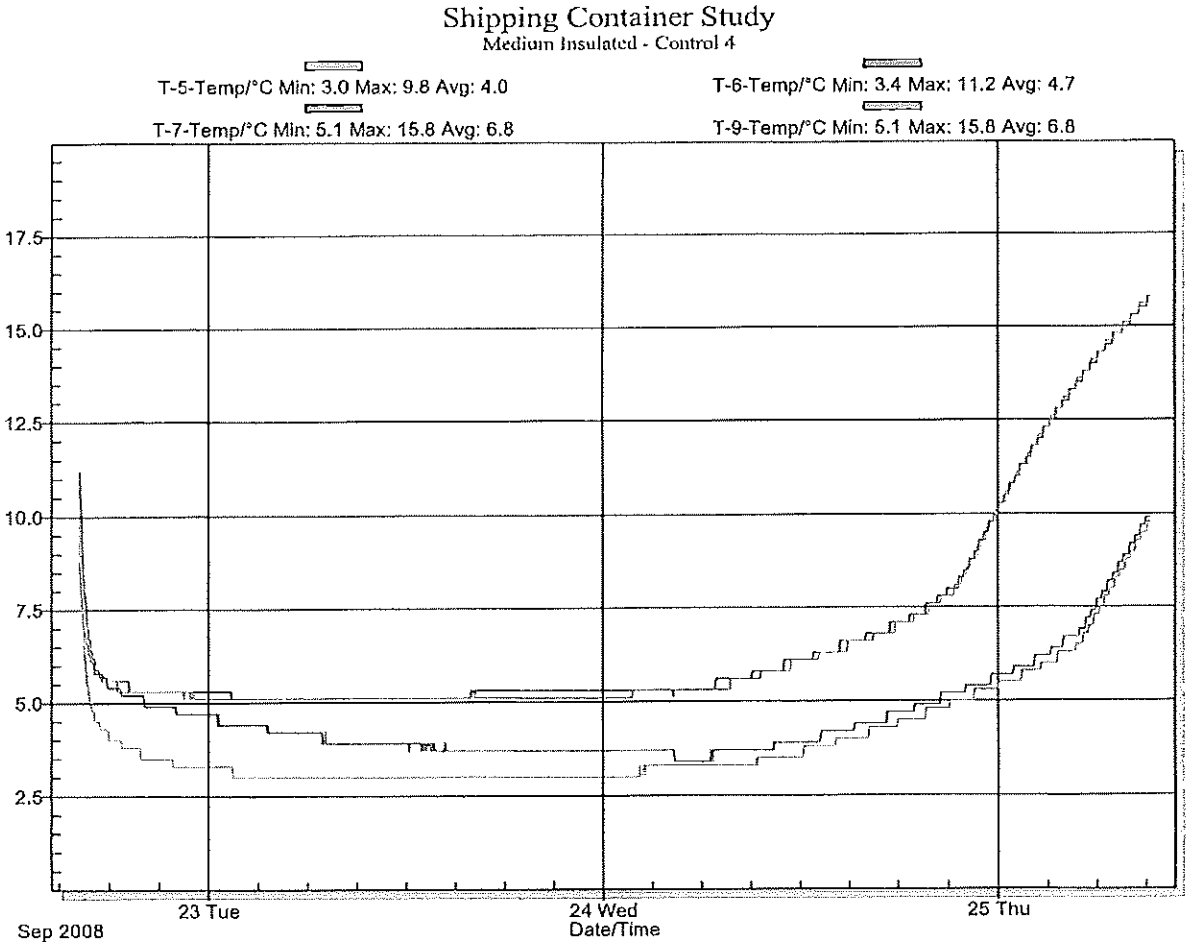
18 Thu
Sep 2008
Date/Time

Appendix 11


Shipping Container Study
Medium Insulated - Control 4
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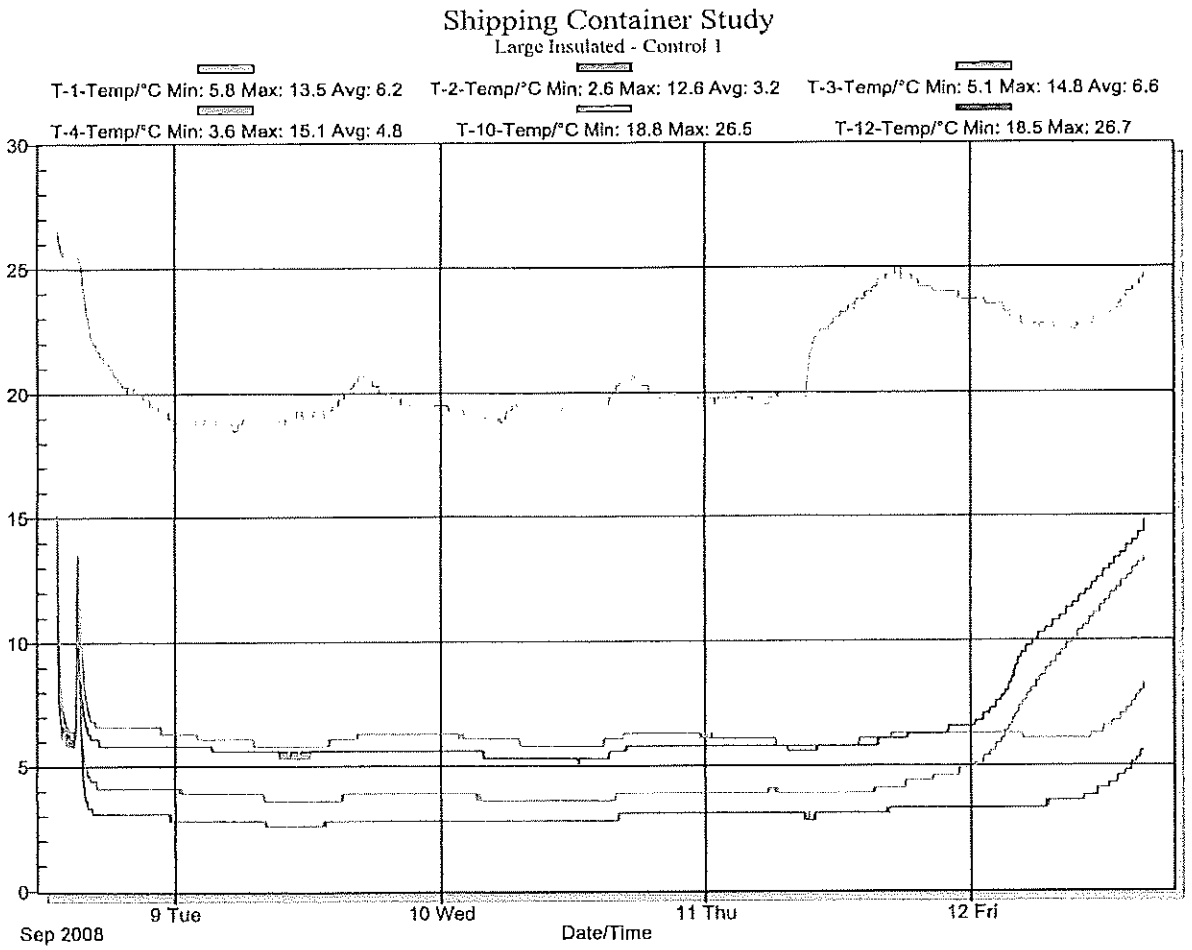
T-6-Temp/°C Min: 3.4 Max: 11.2 Avg: 4.7
T-7-Temp/°C Min: 5.1 Max: 15.8 Avg: 6.8
T-9-Temp/°C Min: 5.1 Max: 15.8 Avg: 6.8
17.5
15.0
12.5
10.0
7.5
5.0
2.5
23 Tue
24 Wed
25 Thu
Sep 2008
Date/Time

Appendix 12


Shipping Container Study
Large Insulated - Control 1
T-1-Temp/°C Min: 5.8 Max: 13.5 Avg: 6.2
T-2-Temp/°C Min: 2.6 Max: 12.6 Avg: 3.2
T-3-Temp/°C Min: 5.1 Max: 14.8 Avg: 6.6
T-4-Temp/°C Min: 3.6 Max: 15.1 Avg: 4.8
T-10-Temp/°C Min: 18.8 Max: 26.5
T-12-Temp/°C Min: 18.5 Max: 26.7
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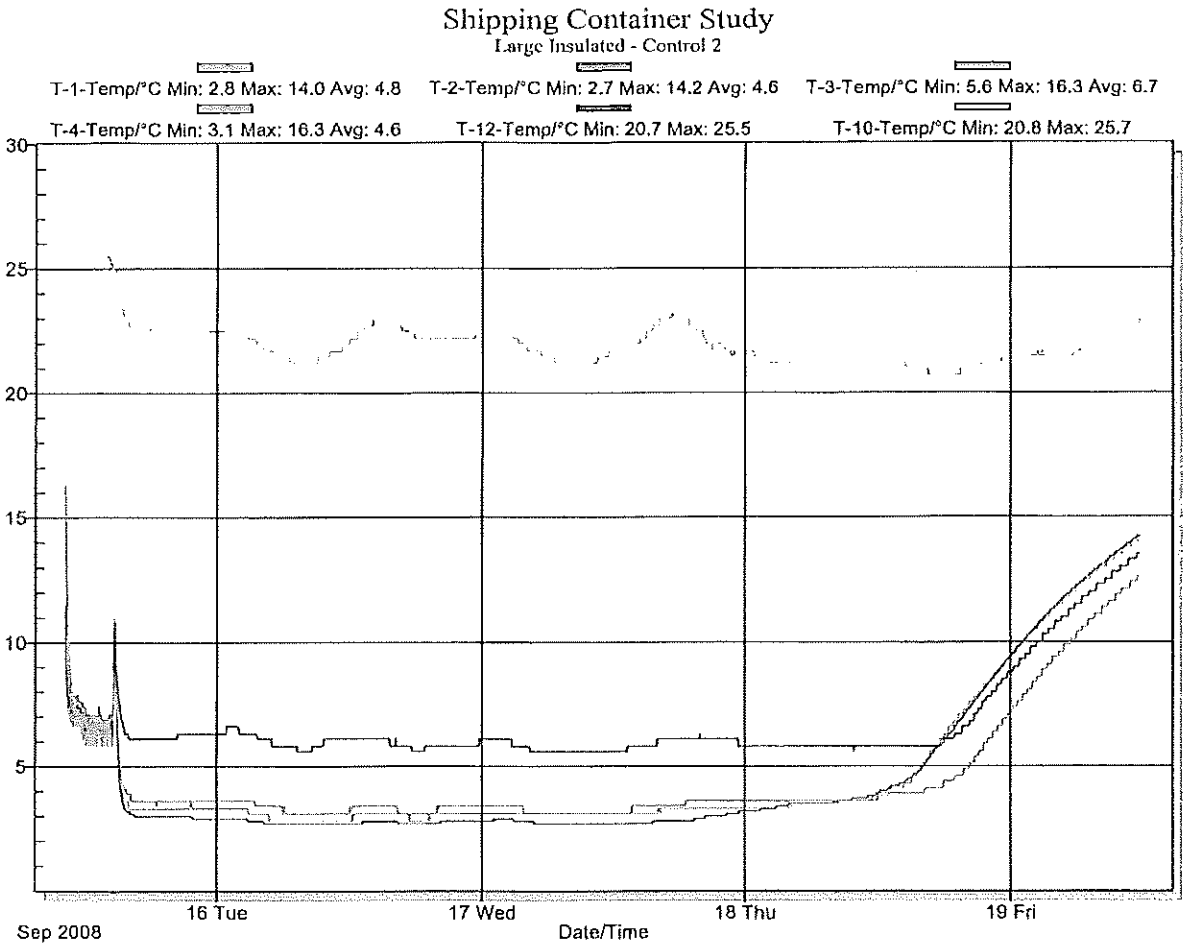
9 Tue
10 Wed
11 Thu
12 Fri
Sep 2008
Date/Time

Appendix 13


Shipping Container Study
Large Insulated - Control 2
T-1-Temp/°C Min: 2.8 Max: 14.0 Avg: 4.8
T-2-Temp/°C Min: 2.7 Max: 14.2 Avg: 4.6
T-3-Temp/°C Min: 5.6 Max: 16.3 Avg: 6.7
T-4-Temp/°C Min: 3.1 Max: 16.3 Avg: 4.6
T-12-Temp/°C Min: 20.7 Max: 25.5
T-10-Temp/°C Min: 20.8 Max: 25.7
30
25
20
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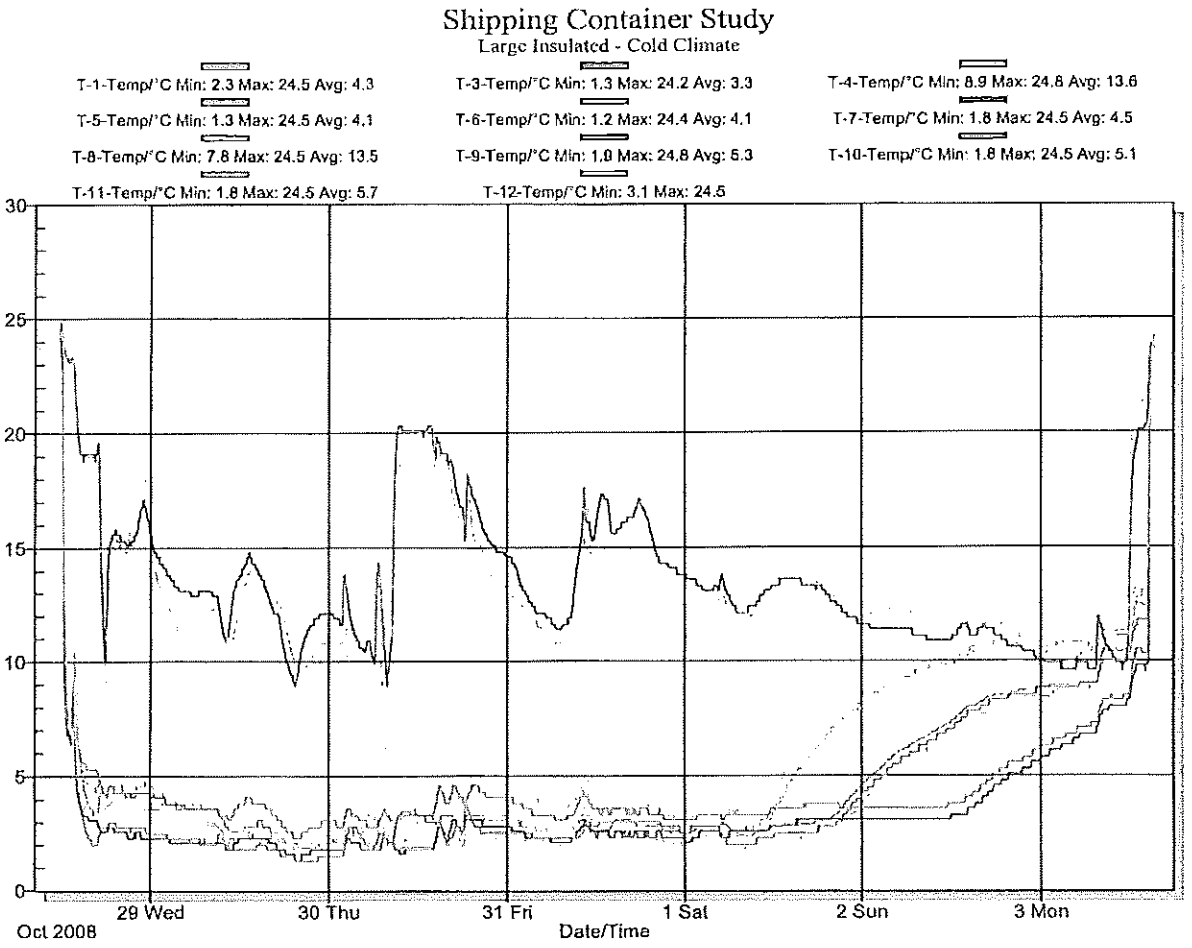
16 Tue
17 Wed
18 Thu
19 Fri
Sep 2008
Date/Time

Appendix 14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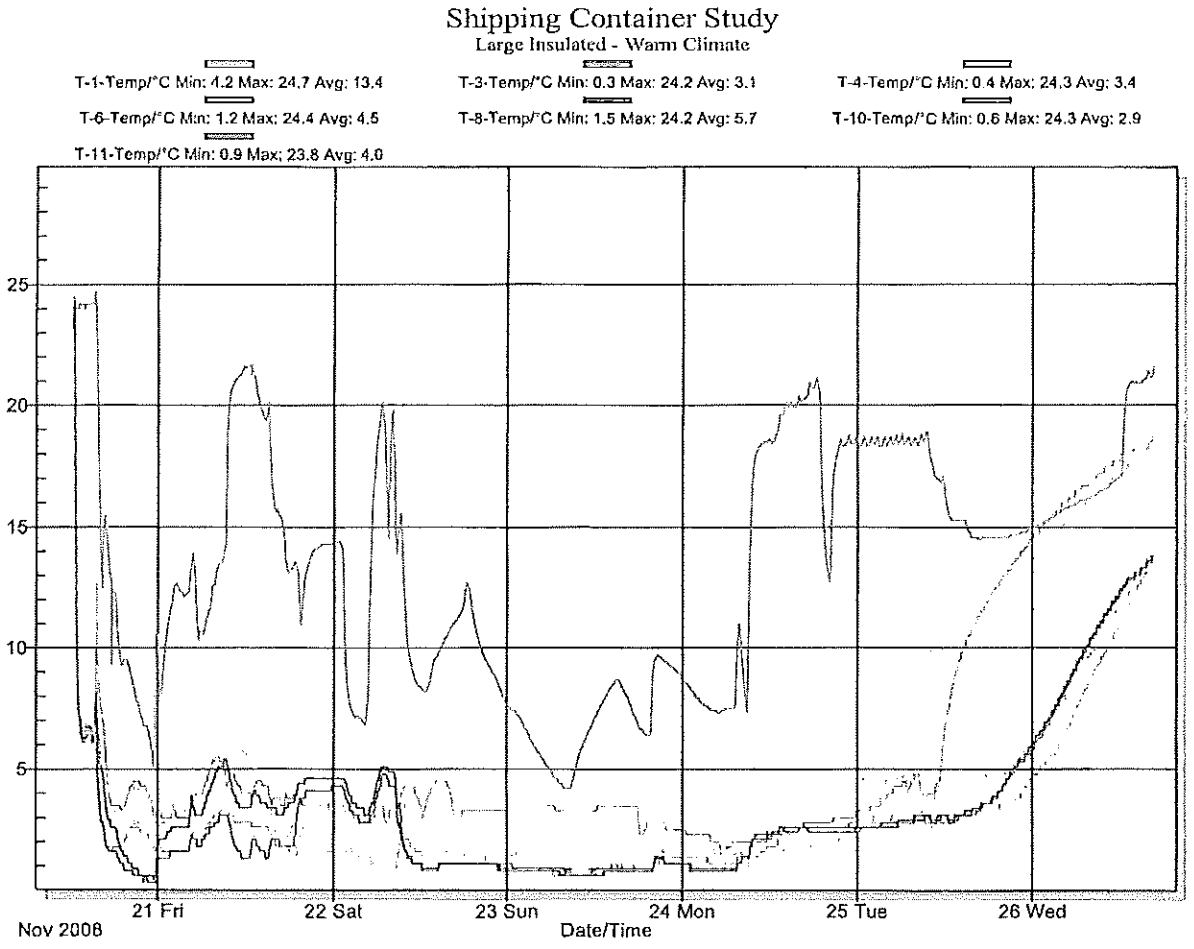
Large Insulated - Cold Climate
T-1-Temp/°C Min: 2.3 Max: 24.5 Avg: 4.3
T-3-Temp/°C Min: 1.3 Max: 24.2 Avg: 3.3
T-4-Temp/°C Min: 8.9 Max: 24.8 Avg: 13.6
T-5-Temp/°C Min: 1.3 Max: 24.5 Avg: 4.1
T-6-Temp/°C Min: 1.2 Max: 24.4 Avg: 4.1
T-7-Temp/°C Min: 1.8 Max: 24.5 Avg: 4.5
T-8-Temp/°C Min: 7.8 Max: 24.5 Avg: 13.5
T-9-Temp/°C Min: 1.8 Max: 24.8 Avg: 5.3
T-10-Temp/°C Min: 1.8 Max: 24.5 Avg: 5.1
T-11-Temp/°C Min: 1.8 Max: 24.5 Avg: 5.7
T-12-Temp/°C Min: 3.1 Max: 24.5
30
25
20
15
10
5
0
29 Wed
30 Thu
31 Fri
1 Sat
2 Sun
3 Mon
Oct 2008
Date/Time

Appendix 15


Shipping Container Study
Large Insulated - Warm Climate
T-1-Temp/°C Min: 4.2 Max: 24.7 Avg: 13.4
T-3-Temp/°C Min: 0.3 Max: 24.2 Avg: 3.1
T-4-Temp/°C Min: 0.4 Max: 24.3 Avg: 3.4
T-6-Temp/°C Min: 1.2 Max: 24.4 Avg: 4.5
T-8-Temp/°C Min: 1.5 Max: 24.2 Avg: 5.7
T-10-Temp/°C Min: 0.6 Max: 24.3 Avg: 2.9
T-11-Temp/°C Min: 0.9 Max: 23.8 Avg: 4.0
25
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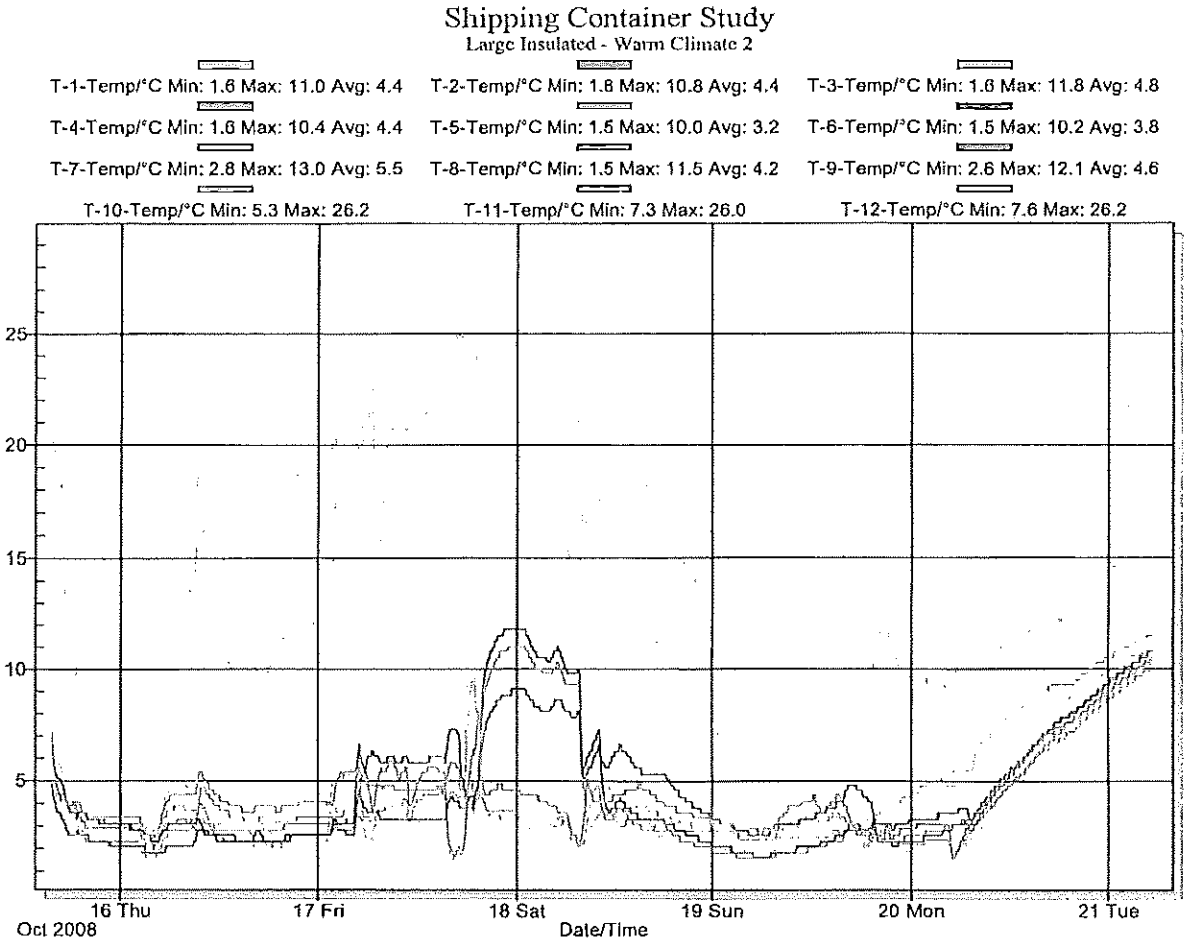
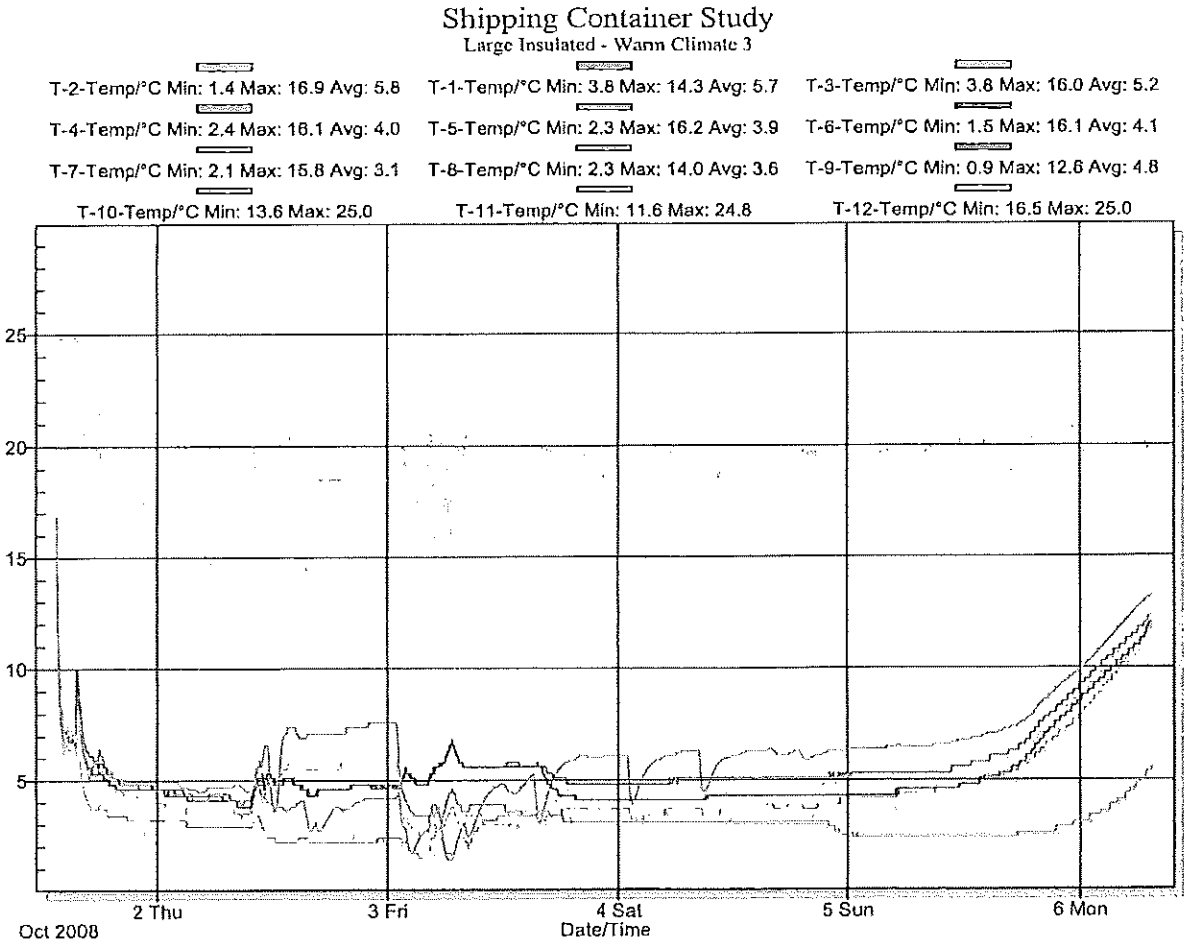
Nov 2008
21 Fri
22 Sat
23 Sun
24 Mon
25 Tue
26 Wed
Date/Time

Appendix 16


Shipping Container Study
Large Insulated - Warm Climate 2
T-1-Temp/°C Min: 1.6 Max: 11.0 Avg: 4.4
T-2-Temp/°C Min: 1.8 Max: 10.8 Avg: 4.4
T-3-Temp/°C Min: 1.6 Max: 11.8 Avg: 4.8
T-4-Temp/°C Min: 1.6 Max: 10.4 Avg: 4.4
T-5-Temp/°C Min: 1.5 Max: 10.0 Avg: 3.2
T-6-Temp/°C Min: 1.5 Max: 10.2 Avg: 3.8
T-7-Temp/°C Min: 2.8 Max: 13.0 Avg: 5.5
T-8-Temp/°C Min: 1.5 Max: 11.5 Avg: 4.2
T-9-Temp/°C Min: 2.6 Max: 12.1 Avg: 4.6
T-10-Temp/°C Min: 5.3 Max: 26.2
T-11-Temp/°C Min: 7.3 Max: 26.0
T-12-Temp/°C Min: 7.6 Max: 26.2
25
20
15
10
5
16 Thu
17 Fri
18 Sat
19 Sun
20 Mon
21 Tue
Oct 2008
Date/Time

Appendix 17


Shipping Container Study
Large Insulated - Warm Climate 3
T-2-Temp/°C Min: 1.4 Max: 16.9 Avg: 5.8
T-1-Temp/°C Min: 3.8 Max: 14.3 Avg: 5.7
T-3-Temp/°C Min: 3.8 Max: 16.0 Avg: 5.2
T-4-Temp/°C Min: 2.4 Max: 16.1 Avg: 4.0
T-5-Temp/°C Min: 2.3 Max: 16.2 Avg: 3.9
T-6-Temp/°C Min: 1.5 Max: 16.1 Avg: 4.1
T-7-Temp/°C Min: 2.1 Max: 15.8 Avg: 3.1
T-8-Temp/°C Min: 2.3 Max: 14.0 Avg: 3.6
T-9-Temp/°C Min: 0.9 Max: 12.6 Avg: 4.8
T-10-Temp/°C Min: 13.6 Max: 25.0
T-11-Temp/°C Min: 11.6 Max: 24.8
T-12-Temp/°C Min: 16.5 Max: 25.0
25
20
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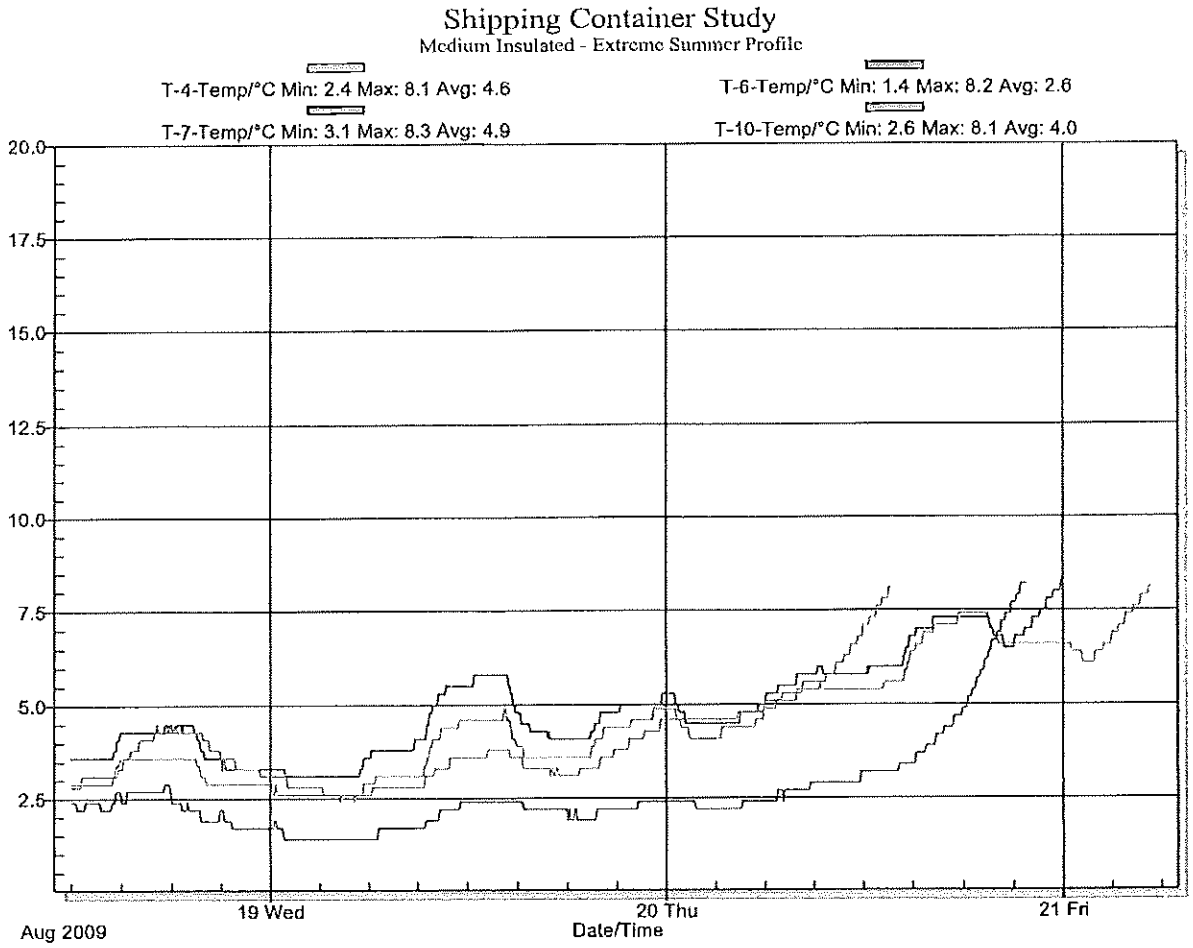
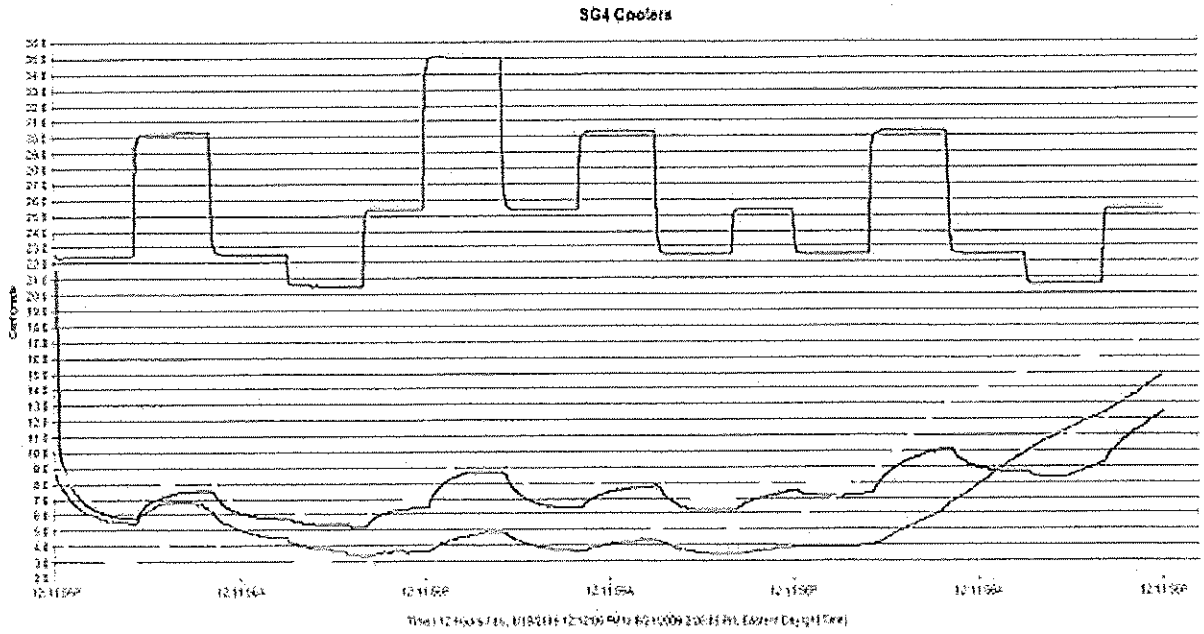
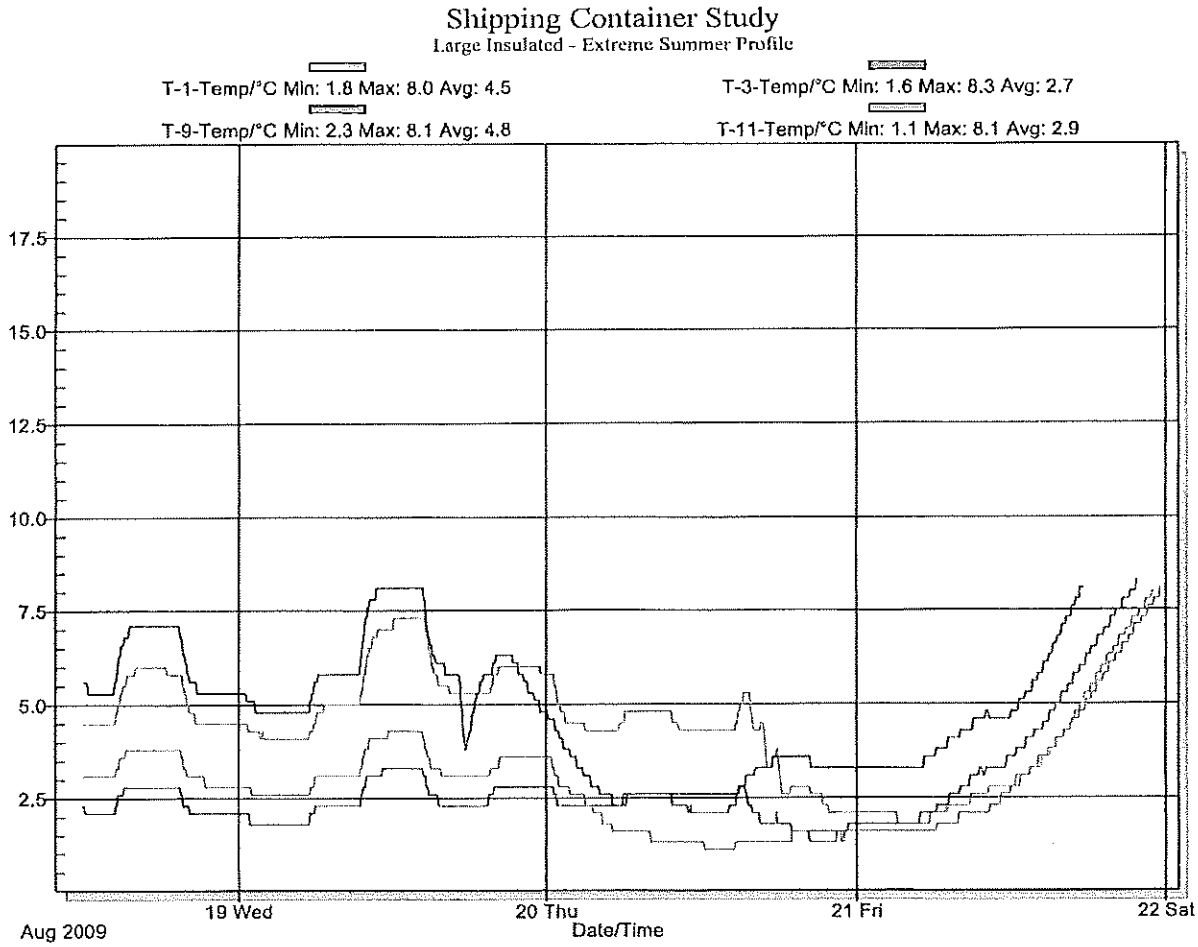
2 Thu
3 Fri
4 Sat
5 Sun
6 Mon
Oct 2008
Date/Time

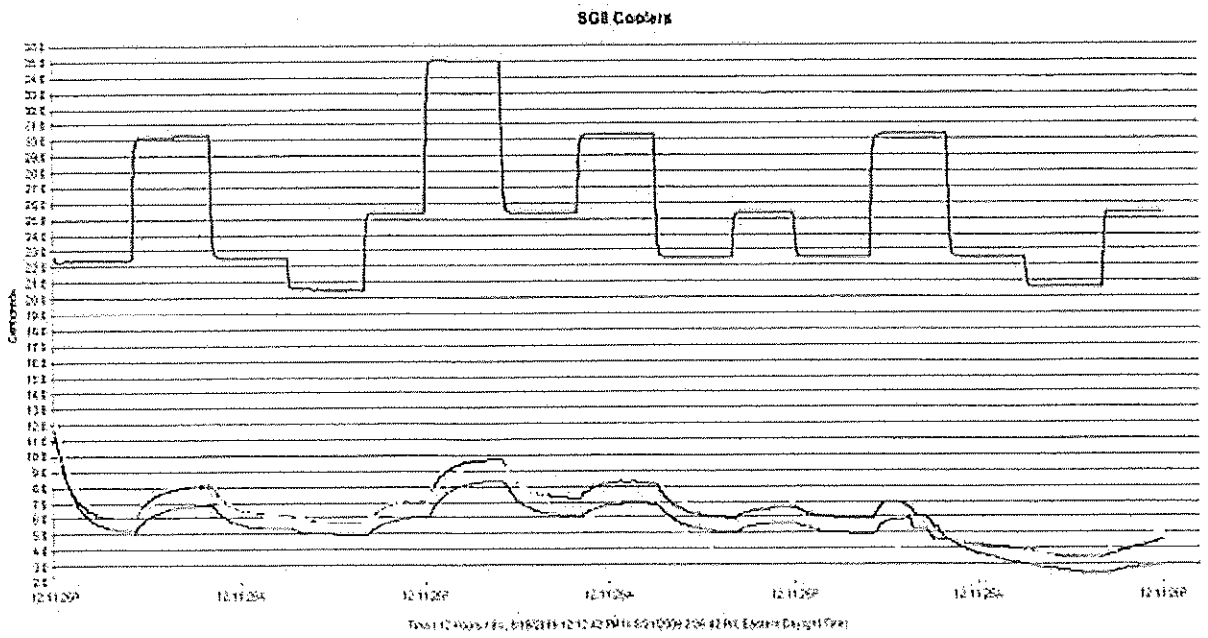
Appendix 18


Shipping Container Study
Medium Insulated - Extreme Summer Profile
T-4-Temp/°C Min: 2.4 Max: 8.1 Avg: 4.6
T-6-Temp/°C Min: 1.4 Max: 8.2 Avg: 2.6
T-7-Temp/°C Min: 3.1 Max: 8.3 Avg: 4.9
T-10-Temp/°C Min: 2.6 Max: 8.1 Avg: 4.0
20.0
17.5
15.0
12.5
10.0
7.5
5.0
2.5
19 Wed
20 Thu
21 Fri
Aug 2009
Date/Time


SG4 Coolers

Appendix 19


Shipping Container Study
Large Insulated - Extreme Summer Profile
T-1-Temp/°C Min: 1.8 Max: 8.0 Avg: 4.5
T-3-Temp/°C Min: 1.6 Max: 8.3 Avg: 2.7
T-9-Temp/°C Min: 2.3 Max: 8.1 Avg: 4.8
T-11-Temp/°C Min: 1.1 Max: 8.1 Avg: 2.9
17.5
15.0
12.5
10.0
7.5
5.0
2.5
19 Wed
20 Thu
21 Fri
22 Sat
Aug 2009
Date/Time


SGB Coolers

Appendix 20

		BSTA	Standard	Summer	Profile	48 Hours			
5 hours	5 hours	5 hours	5 hours	4 hours	5 hours	5 hours	5 hours	5 hours	4 hours
18°C	22°C	18°C	16°C	20°C	35°C	20°C	25°C	18°C	20°C
		BSTA	Elevated	Summer	Profile	48 Hours			
22°C	30°C	22°C	20°C	25°C	35°C	25°C	30°C	22°C	25°C
27°C	35°C	27°C	25°C	30°C	40°C	30°C	35°C	27°C	30°C

BSTA profiles were developed utilizing actual shipping temperature data on a year round basis with the periods:
October to March representing the **Winter Profiles** and
April to September representing the **Summer Profiles**.

While these profiles reflect standard parcel shipping practices within the contiguous 48 states, they are averages and cannot be construed as all enclusive of conditions that a package and it's contents may encounter. Origination and destination locations, routes, times and equipment are just a few of the variables that can affect shipments.

Considering these variables, BSTA offers three levels of temperature protocols to enable sites to develop appropriate and progressive packaging solutions
Standard- representing less severe months and shipping environments
Elevated- representing average broad spectrum conditions
Extremo- representing colder months and shipping environments

Clients that wish to develop protocols more representative of their climate and shipping methodologies are encouraged to developed their own protocols.

The BSTA or Biological Specimen Transportation Association, is a group that came together to develop shipping temperature profiles that could be used in the medical industry.

Appendix 21

COUNTRY SHIPPING GUIDE

Destination	Transit Time	Size*	Destination	Transit Time	Size*
Argentina	24-48	Medium	Kuwait	48-72	Large
Azerbaijan	48-72	Large	Malaysia	48-72	Large
Bahrain	48-72	Large	Mexico	24-36	Medium
Barbados	24-48	Medium	Nicaragua	24-48	Medium
Beruit	24-48	Medium	North Africa	48-72	Large
Bolivia	24-72	Large	Nova Scotia	<24	Medium
Bolivia	24-48	Medium	Oman	48-72	Large
Brazil	24-48	Medium	Pakistan	48-72	Large
Canada	<24	Medium	Peru	24-48	Medium
Chile	24-48	Medium	Puerto Rico	<24	Medium
Costa Rica	24	Medium	Quebec	24	Medium
Cyprus	24-48	Medium	Romania	48-72	Large
Dominican Rep	24-48	Medium	S.Africa	48-72	Large
Ecuador	24-48	Medium	Saudi Arabia	48-96	Large
Egypt	48-72	Large	Senegal	24-48	Medium
El Salvador	24-48	Medium	Singapore	24-72	Large
Finland	48-72	Large	South Africa	48-72	Large
Germany	48-72	Large	Spain	24-48	Medium
Ghana	24-48	Medium	Syria	48-72	Large
Greece	48-72	Large	Taiwan	24-72	Large
Guatamala	24-48	Medium	Tanzania	48-72	Large
Honduras	24-48	Medium	Thailand	48-72	Large
Iceland	24-48	Medium	Trinidad	24-48	Medium
India	48-72	Large	Turkey	48-72	Large
Indonesia	48-72	Large	UAE	48-72	Large
Israel	24-48	Medium	UK	24-48	Medium
Jamaica	24-48	Medium	Uruguay	24-48	Medium
Jamaica	24-48	Medium	USA**	<24	Medium
Japan	24-72	Large	Uzbekistan	48-72	Large
Jordan	24-48	Medium	Venezuela	24-48	Medium
Korea	24-48	Medium	Vietnam	48-72	Large

***For shipments to destinations demonstrated above to require a medium shipping container, upgrade to a large shipping container if shipping multiple corneas in the shipment due to reduced volume of coolant.**

****For local shipments a small shipping container should be fine. A medium shipping container should be used for most other shipments to allow for possible shipping problems.**

Note: If extremely high temperatures are expected to be encountered during transport (e.g. shipments to Saudi Arabia in July), increase the size of the container and the volume of coolant.

Interim Report

Shipping Container Validation
For SafeGuard SG-8 Shipper

PREPARED FOR

VISION SHARE

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Apex, NC 27502

PREPARED BY

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Quality Assurance Coordinator, SightLife

Thomas D. Lindquist, PhD, MD
Medical Director, SightLife

DATE
06/01/09

PROPRIETARY INFORMATION

Shipping Container Validation SG-8

1.0 INTRODUCTION

1.1 In the daily operation of eye banks, the transportation of corneas is an essential part of the supply chain. Current industry standards require that eye banks use a packaging method designed to prevent freezing of tissue and to maintain cool storage such that the package content demonstrates residual coolant in effect at the time of use, removal to mechanical storage or replacement of the coolant. This study was designed to determine the interval of cooling effect of the Safeguard SG-8 shipping container in controlled and non-controlled shipping environments.

2.0 PURPOSE

2.1 Current Good Tissue Practice for Manufacturers of Human Cellular and Tissue-Based Products under 21 CFR 1271.195 requires establishments to identify any environmental conditions that require monitoring and *control.* This rule requires that procedures be written for environmental control and monitoring activities of systems where an environmental condition could have an adverse effect on the tissue-based product, causing contamination or cross-contamination.

2.2 Eye Bank Association of America Medical Standard L2.000 requires that an eye bank use a packaging method designed to maintain cool storage where the package content demonstrates remaining coolant effect at the time of use or removal to mechanical storage or replacement of the coolant and to prevent freezing.

2.3 This report validates that when current practices and procedures are followed for shipping corneal tissue and blood samples to and from an eye bank, locally, nationally and internationally and serology testing laboratory domestically proper cooling requirements can be met and exceeded.

2.4 This study was designed to determine the interval of cooling effect of the Safeguard SG-8 shipping container in controlled and non-controlled shipping environments.

3.0 SCOPE

3.1 In this study, we assessed the suitability of the Safe-Guard brand shipping container SG-8 and packing procedures typically used by the eye banking industry in the United States.

3.2 This report encompasses the results related to packing, shipping and monitoring of temperature data loggers during actual shipping events that simulated current practices utilized by industry for packing and shipping of corneal tissue.

4.0 MATERIALS

4.1 Summary: The Safeguard SG-8 shipping container was packed following industry practices with wet ice quantities that varied between 3500-4800 grams. Commercially available temperature monitors were packaged as cornea chambers

for shipping. The packages were subjected to controlled environments (regulated office) or non-controlled (field trials) environments (i.e. couriers, airlines, FedEx to different climates). The control group was given limited exposure to temperature variation in order to establish a base line cooling effect at warm temperature (assuming no external cooling). The shippers were continuously monitored internally and externally using data loggers recording data (time & temperature) every 2 minutes. The data was evaluated to determine time interval that the terminal cooling effect remained above 8°C. The time interval to weight of ice was used to determine cooling effect of the box. The non-controlled (field trials) group was exposed to various external temperatures, experienced by actual conditions encountered during transport. Due to significant regional temperature differences, we identified differing warm and cold climates in the United States and shipped packages to these regions. The data was collected the same for both regions. Depicted are graphs for controlled and non-controlled shipping events.

4.2 SafeGuard shipping boxes and inserts:

a. See Appendix 1 SG-8 *Shipping Container Dimensions*

b. These shipping boxes feature a thick-walled container of 1.5", expanded polystyrene foam. A tight fitting lid plug also ensures thermal efficiency.

c. SG-1 - inside length 8", inside width 6", inside depth 4.25"

d. SG-4 - inside length 8", inside width 6", inside depth 9.75"

e. SG-8 - inside length 11", inside width 8.5", inside depth 9.25"

f. Outer cases are 200-lb. test corrugated cardboard

4.3 Dickson SK500 Temperature Data Loggers:

a. Temperature Accuracy ±1.8F (±1C) over range -4 to +158°F (-20 to +70°C)

b. Temperature Range -4 to 158F, -20 to 70C

c. Calibration - is the process of making a zero (low scale) adjustment so that it matches exactly to a known standard, and a separate span (high scale) adjustment that also matches the unit exactly to a known standard. These two independent adjustment procedures are repeated until the unit matches the known standard, within its allowed specification. After this process is complete, the unit is accurate throughout its full measurement range.

d. Approval – CE approved

e. Data Logger Calibration: June, 2008

4.4 Foam inserts

4.5 Plastic bag(s)

a. For the foam insert

b. Dickson SK500 data logger (4" x 7" zip lock)

c. For wet ice (12" x 18")

4.6 Packing Tape

4.7 Ice bag sealer is an American International Electronics' Impulse Sealer with Magnet Model AIE-405MC

4.8 Ice Scoop is a 24 oz - 710 ml

4.9 Scale is a Francotyp-Postalia P150 with a weight capacity of 0.2 oz. to 150 lb. and accuracy of +/- 0.2 oz. from 0-4 lb. and +/- 0.5 oz. from 4-150 lb.

4.10 Wet ice is from a Manitowoc model QM-45, self contained air cooled dice cube ice maker

5.0 PACKING AND SHIPPING POLICIES AND PROCEDURES

5.1 Vision Share Facilities are located in various regions/climates nationwide.

5.2 Generic packing and shipping procedures were followed for this validation and should return similar results when followed.

5.3 Procedures used in this validation are described as part of this validation report and are also available at the Vision Share Corporate office.

6.0 SAMPLING SCHEME

6.1 This report includes a data set for winter months (October – March). A data set for summer months (April – September) will follow when completed as stated in the protocol.

6.2 The sampling frequency was to consist of at least 10 sampling events in a warm climate, 10 sampling events in a cold climate and 10 sampling events in a controlled ambient environment during winter months (October – March). The sampling frequency for summer months (April – September) will follow when completed as stated in the protocol.

6.3 A sampling event consisted of packing, shipping and returning the shipping box packed with various quantities of wet ice and data loggers to shipper.

6.4 Sampling events were collected during actual shipping events, measuring time and temperature of the shipping box's internal and external (ambient) temperature.

7.0 METHODS

7.1 SUMMARY: The Safeguard SG-8 shipping container was packed following industry practices with wet ice quantities that varied between 3500-4800 grams. Commercially available temperature monitors were packed as corneas in chambers are packed for shipping. The packages were subjected to controlled environments (temperature regulated office) and/or un-controlled environments (i.e. couriers, airlines, FedEx to different climates). The temperature monitors recorded data every

2 minutes. The data was evaluated until the terminal cooling effect remained above 8 ℃.

7.2 Data Logger:

a. Using Dickson software program the data logger to:

1. Set data logger to record temperature at no less than 1 minute and no longer than every 5 minutes
2. Record without looping (writing over previous data when full)
3. Set appropriate date and time
4. Set measurement to Celsius

b. Reset the data logger

c. Place the logger in a foam block

d. Seal the data logger and foam block in a plastic bag

e. Place data logger in tissue refrigerator to pre-cool prior to packing (for a minimum of 30 minutes)

7.3 Shipment:

a. See Appendix 2: *SG-8 Shipping Container*

b. Inspect shipping container SG-8, ensuring that it is labeled in accordance with industry standards.

1. Seal data logger in a plastic bag.
   i. Sealed plastic bag is used to prevent possible damage of data logger by moisture.

b. Place foam block with sealed data logger into a polystyrene box.

1. Foam block prevents excessive movement within the polystyrene box.

c. Place one layer of paper towels over top of the foam block to insulate the data logger from direct contact with the wet ice and to absorb any condensation or leakage that may occur.

d. Place wet ice sealed in plastic bag(s) into SG-8 shipping container.

1. Ensure enough wet ice is used to fill shipping container.
2. Wet ice is ice at its melting point. If ice is below its melting point, add water to begin melting process.
3. Measure individual bags of ice and record a total weight of wet ice used.

e. Place the lid on the Styrofoam box and secure with packing tape.

1. Seal around lid of polystyrene box according to airline regulations and put in a box shell.

2. A secured box provides a waterproof container and preserves coolness

f. Use a box shell, seal lid and all edges with packing tape.

1. Secures box against potential tampering and further prevents possible leakage of fluids.

g. Place proper handling labels on the outside of the shipping container indicating safe shipping and storage methods.

1. Handling labels clearly identify the statement "DO NOT FREEZE" to prevent mistakes in transit and to keep the shipping box from freezing.

6.2 Measurements

a. Wet ice was measured by weight prior to packing using a calibrated scale.

b. Interval temperature measurements were performed by data logger(s).

c. Time was recorded with temperature via data logger(s).

7.0 PROTOCOL CHANGES

7.1 The following protocol changes, revisions and reasons for the change are documented in this section, and will remain part of the permanent file for this study.

7.2 The Researcher was notified concerning changes, and revisions as the event occurred, none have an effect on the validity of this study.

8.0 DATA RETENTION

8.1 A copy of this report and the raw data will be kept on file at the Vision Share corporate office for 10 years from the date of study completion.

9.0 DATA COLLECTION AND EVALUATION

9.1 Data was collected and summarized on computer generated worksheets.

9.2 Recorded the time interval from the start of packaging until temperature readings from the data loggers was consistently above 8℃.

9.3 Correlated the time intervals from start to above 8℃ with weight of ice.

a. Graph the volume of ice to time

b. Determine the linear regression

c. Use the equation of the line to determine correlation of ice quantity to time of refrigeration at or below an average of 8℃.

10.0 STATISTICAL ANALYSIS

10.1 Statistical analysis was performed on the collected data points.

10.2 The controlled shipping group consisted of 16 recorded events with an external temperature average of 21.8℃ and a range of 7℃. Ice quantity variation per shipping box had a mean 4438.5 grams, mode of 4310 grams, and range of 740

grams. The ice from all the controlled events totaled 71016.6 grams of wet ice and produced 82231.0 minutes of cooling effect at or below 8°C.

10.3 The controlled shipping group minutes of cooling effect at or below 8°C gives a mean of 1.2 minutes per gram of wet ice.

10.4 The non-controlled (field trials) shipping group consisted of 15 recorded events with an external temperature average of 15.1°C, and a range of 20.5°C. Ice quantity variation per shipping box had a mean 4017.1 grams, mode of 4167.4 grams, and range of 1525.2 grams. The ice from all non-controlled events totaled at 56239.7 grams of wet ice produced 104177.0 minutes of cooling effect at or below 8°C

10.5 The non-controlled shipping group minutes of cooling effect at or below 8°C gives a mean of 1.9 minutes per gram of wet ice.

10.6 The control group produced a result of grams of ice to time recorded to maintain a temp at/or below 8°C resulting in a linear regression equation of $y=0.5892x+1410.3$. (y is grams of ice, x is minutes).

10.7 The non-controlled (field trials) group produced a result of grams of ice to time recorded to maintain a temp at/or below 8°C resulting in a linear regression equation of $y=0.5388x+8.0263$. (y is grams of ice, x is minutes).

10.8 The Safeguard SG-8 shipping container provided cooling effect at or under 8°C for an average of 1.2 and 1.9 minutes per gram of wet ice with external temperatures ranges from 21.8°C to 15.1°C respectively. With 4500 grams of packaged wet ice and an average ambient temperature of 15.1°C, the cooling effect lasted 138.9 hours. With 4500 grams of packaged wet ice and an average ambient temperature of 21.8°C, the cooling effect lasted 87.4 hours.

11.0 SUMMARY / CONCLUSION

11.1 Measuring internal temperature, amount of ice, and external temperature, allowed us to develop a predictive mathematical model. Modeling can greatly improve shipping practices by providing accurate information on expected internal temperatures at various external temperatures.

11.2 This model will help eye banks make decisions on how to properly package and ship corneas locally, nationally and internationally which may improve outcomes on corneal transplantation. The equations do not work outside of the ranges studied. For example, placing only 50 grams of ice will not yield an appropriate cooling time, and 7000 grams of wet ice is unlikely to fit within the volume of the shipping container.

11.3 Additionally, this study did not evaluate quantities of ice blocks that have started the melting process. We found the Safeguard SG-8 shipping container adequate for shipping corneas locally, nationally and internationally. It maintains proper cooling effect when the appropriate grams of wet ice are packaged for the needed time interval. Key considerations are temperature of shipping route, destination and quantity of wet ice. This assures that the amount of cooling effect over time will suffice.

12.0 REGULATORY STATEMENT

12.1 The study referenced in this protocol is conducted in compliance with Current Good Tissue Practice for Manufacturer's of Human Cellular and Tissue-Based Products (21CFR1271.195).

13.0 REFERENCES

13.1 Food and Drug Administration's 21 CFR 1271.195 Good Tissue Practice Regulations

13.2 Food and Drug Administration's 21CFR600.15 Biological Products, Temperatures during shipment

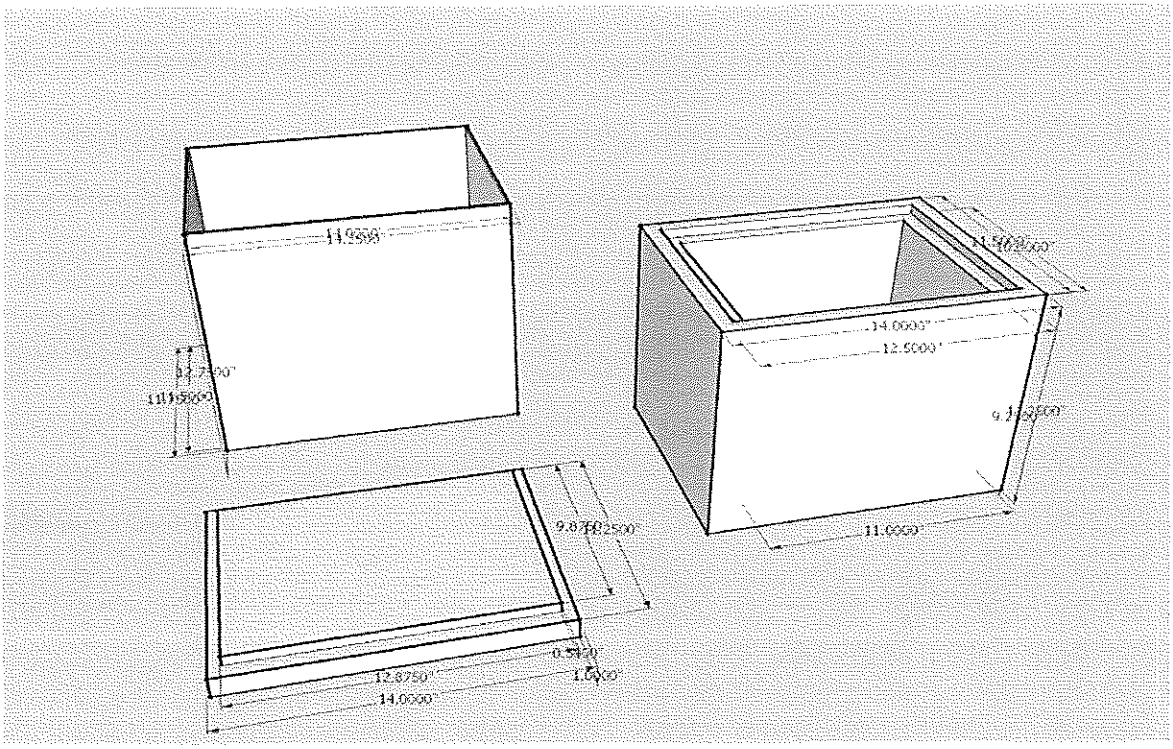
13.3 EBAA Medical Standards (November 2008) L2.000 Packaging, Sealing and Packing for Transport

14.0 REPORT APPROVAL

Director of Regulatory Affairs and Contracts	Date

Appendix 1

SG-8 Shipping Container Dimensions:

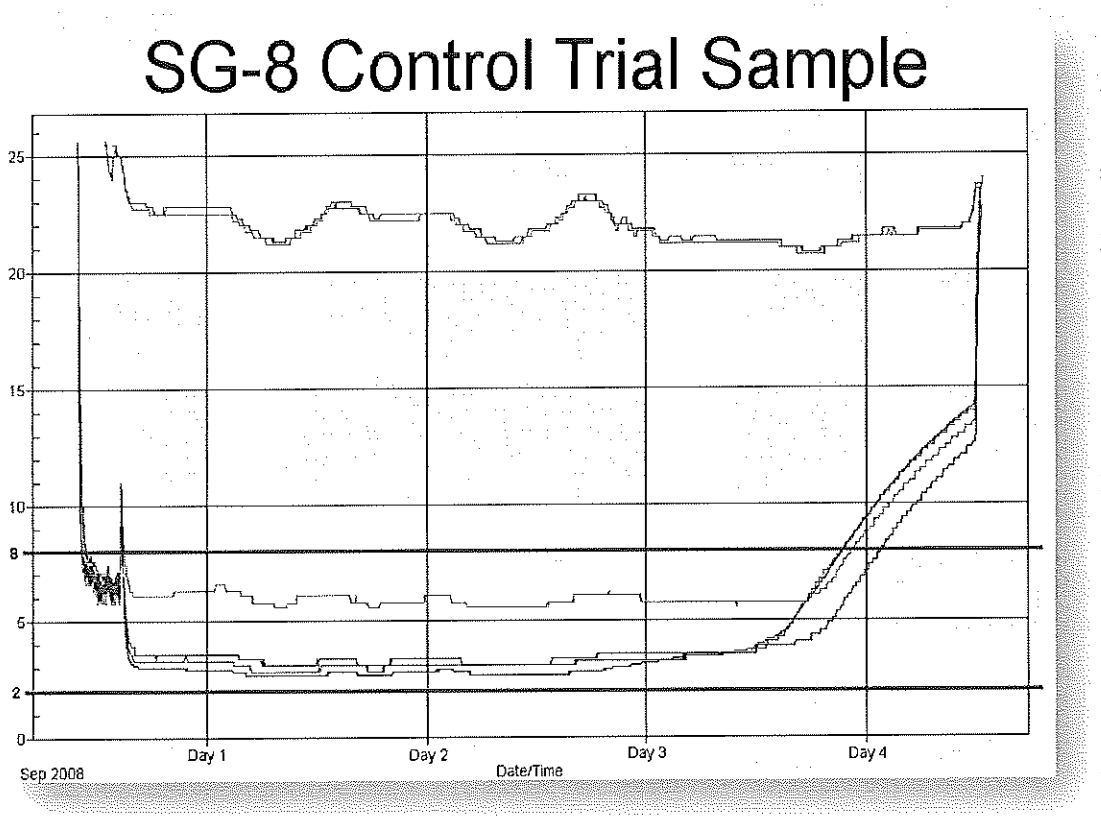


Appendix 2

SG-8 Shipping Container

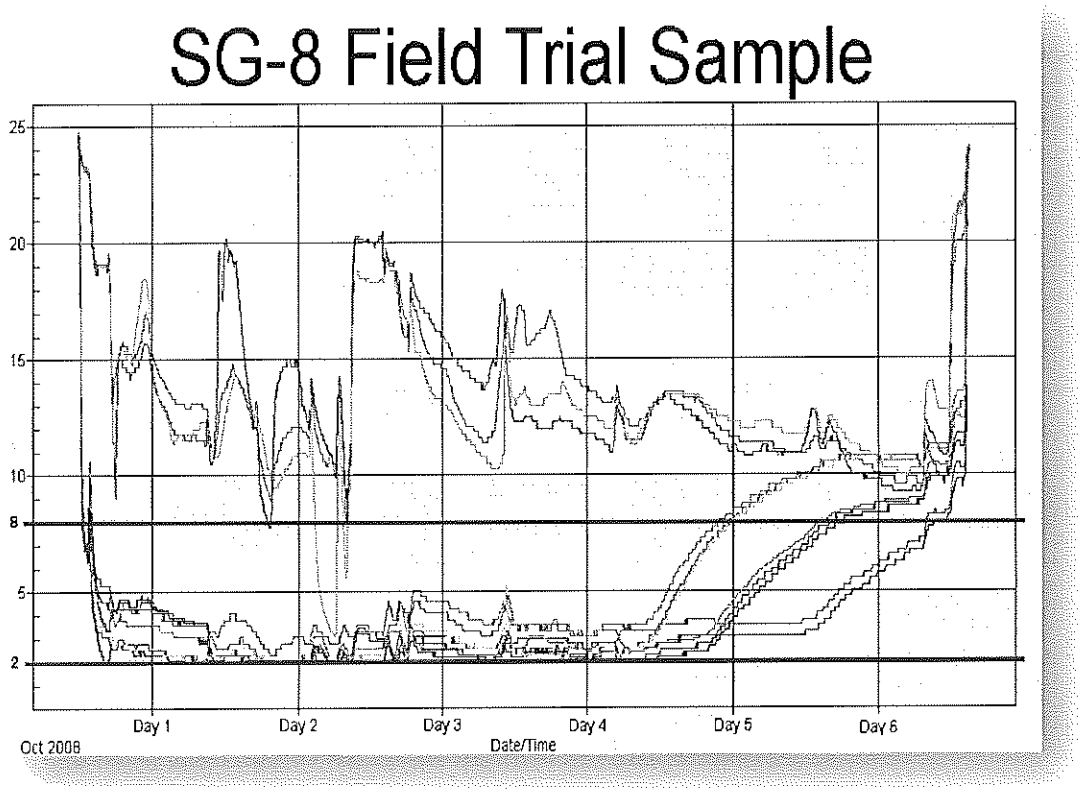
Appendix 3

Control Group Data Sample



Appendix 4

Field Trial Data Sample



Appendix 5

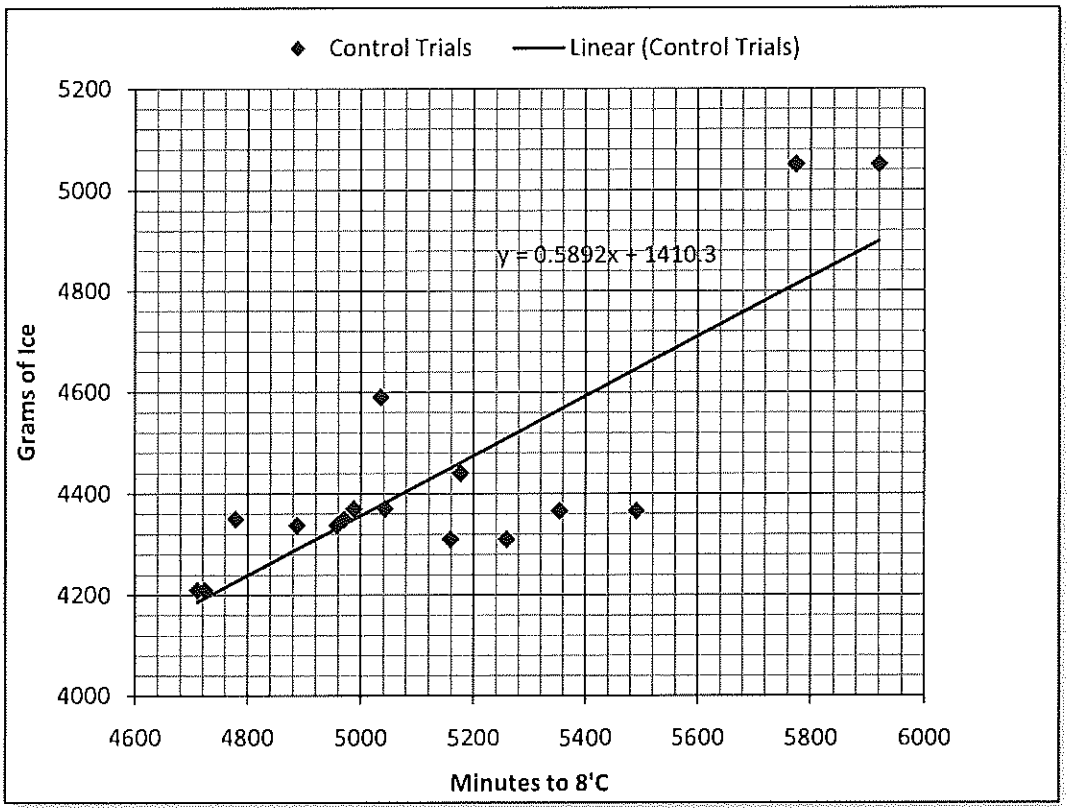
Trial Results

Range	Control Trials	Field Trials
Average Temperature (℃)	21.8	15.1
Minimum Temperature (℃)	18.7	4.2
Maximum Temperature (℃)	25.1	26.1
Average minutes/grams of ice	1.2	1.9
Regression of minutes/grams of ice	y=0.5892x + 1410.3	y=0.5388x + 8.0263

Appendix 6

Graphs of Minutes/Grams of Ice

Control Graph



Appendix 7

Graphs of Minutes/Grams of Ice

Control Graph