## INTRODUCTION

Validation is defined as the process of establishing documented evidence that provides a high degree of assurance that a product, service, or system accomplishes its intended requirements and often involves acceptance and suitability with external customers. Validation is a crucial element in a quality management system and is guided by ISO 9000 Quality Standards (ISO15198:2004), the Code of Federal Regulations (21CFR), Canadian Standards Association CSA Z902-04 Standards for Blood and Blood Components and the Canadian Society for Transfusion Medicine, Standards for Hospital Transfusion Services.

Canadian Blood Services, as one of the two blood providers for Canada has established that less than four percent (4%) of eligible Canadians donate blood. Yet the demand for blood products increases each year. This valuable resource is obtained from volunteer blood donors who altruistically give of their time to assist in the health care of Canadians.

In 1997, British Columbia developed a Regional Redistribution Program. The objective was to reduce blood outdating at isolated low-utilization blood banks and redistribute to higher use hospitals. Since then, BC has reduced blood wastage from nine percent (9%) to less than three percent (2.9%) in 2003. The net result is that thousands of blood products have been salvaged each year.

It has been well documented through inventory management reports that there is significant product loss due to outdating of components. Due to the geographical demography of the province of Newfoundland and Labrador, the development and validation of a process that permits inter-hospital transfer supports the ability to transfer blood components from areas of lesser utilization to areas of higher utilization thus reducing product loss and providing better fiscal management of a valuable resource. CSA Standards state that a transport system shall ensure that whole blood and blood components remain within environmental specifications at all times.

An environmental scan of provincial programs identified that there were many types of transfer programs in use throughout the country. Some of these programs involved the use of shipping containers that had not been validated, or in some instances, operating procedures had been customized to meet local needs. As a result the Newfoundland and Labrador Provincial Blood Coordinating Program launched an initiative to procure and validate a suitable shipping container and develop the required documentation to assist provincial hospitals in participating in an Inter-Hospital Transfer Program (IHTP).
The benefits of such a project include:

- Better inventory management
- Better utilization of a scarce resource
- Compliance with requirements
- Reduced product loss

- Safe, validated and efficient mechanism to transport products
- Savings related to inventory management
    - It is estimated that product loss due to outdating could be reduced significantly with the implementation of inter-hospital transfer of products

In May 2007, a meeting of the Provincial Blood Coordinating Program Offices was held in Nova Scotia. At that time, the Newfoundland and Labrador Provincial Blood Coordinating Program announced its intention to proceed with the development of an Inter Hospital Transfer Program for the province. The participants at the meeting were interested in the project and wished to become involved. As a result, the Inter Hospital Transfer Working Group (IHTWG) was formed. Validation protocols, operating procedures, forms and training material were developed and the validation process began.

## PRODUCT EVALUATION

### Shipping Container

Shipping containers and temperature monitoring devices were evaluated by document review from various vendors.

Some of the key elements in product selection were: the shipping container would be able to withstand a wide temperature range of operation, that it must be of a suitable size that hospitals would be able to inventory and that the use of such a container would have a simple packing scheme to accommodate various temperature ranges. The shipping container would also have to be of an acceptable weight that when full would not present occupational hazards to employees.

The Golden Hour 24/2 Shipping Container has been validated in a laboratory setting to validate the manufacturer's claim that the shipping container will maintain the temperature of red blood cells between $1^0$C and $10^0$C for one to two days.
The shipping container consists of a removable Thermal Isolation Chamber (TIC)™ with an integrated 4ºC Phase Change Material (PCM) that is preconditioned in a -18ºC to -40°C freezer for expected warm ambient temperatures (summer profile). The shipping container is preconditioned in a 6ºC refrigerator for expected cold ambient temperatures (winter profile). The shipping container has a payload of 2 liters and is able to contain four units of concentrated red blood cells. The compact size of the container makes it easy to handle, pre-condition and inventory. The shipping container lid provides easy to follow instructions for use in both the summer and winter profiles.

***Figure 1: Golden Hour 24/2 Shipping Container***

http://www.mnthermalscience.com/products.htm

**Temperature Monitoring Device**

Temperature monitoring devices were used to monitor the ambient temperature as well as the internal temperature of the containers when shipping a minimum and maximum payload of one and four units, respectively. Initially two types of dataloggers were used in preliminary tests to assess user friendliness and to consider datalogger options. After several preliminary tests, it was decided to use the Global Sensors Log Tag Analyzer system. Calibration certificates were obtained for the log tags used.
Note: The preliminary tests were not included as part of the validation test.

***Figure 2: Global Sensors Log Tag Analyzer***

**http://www.global-sensors.com/**

The Log Tag analyzers were configured to measure the temperature at one minute intervals. The Alert indicators were set to record readings below 1°C and above 10°C after 1 consecutive reading even if the readings returned within the alert range.

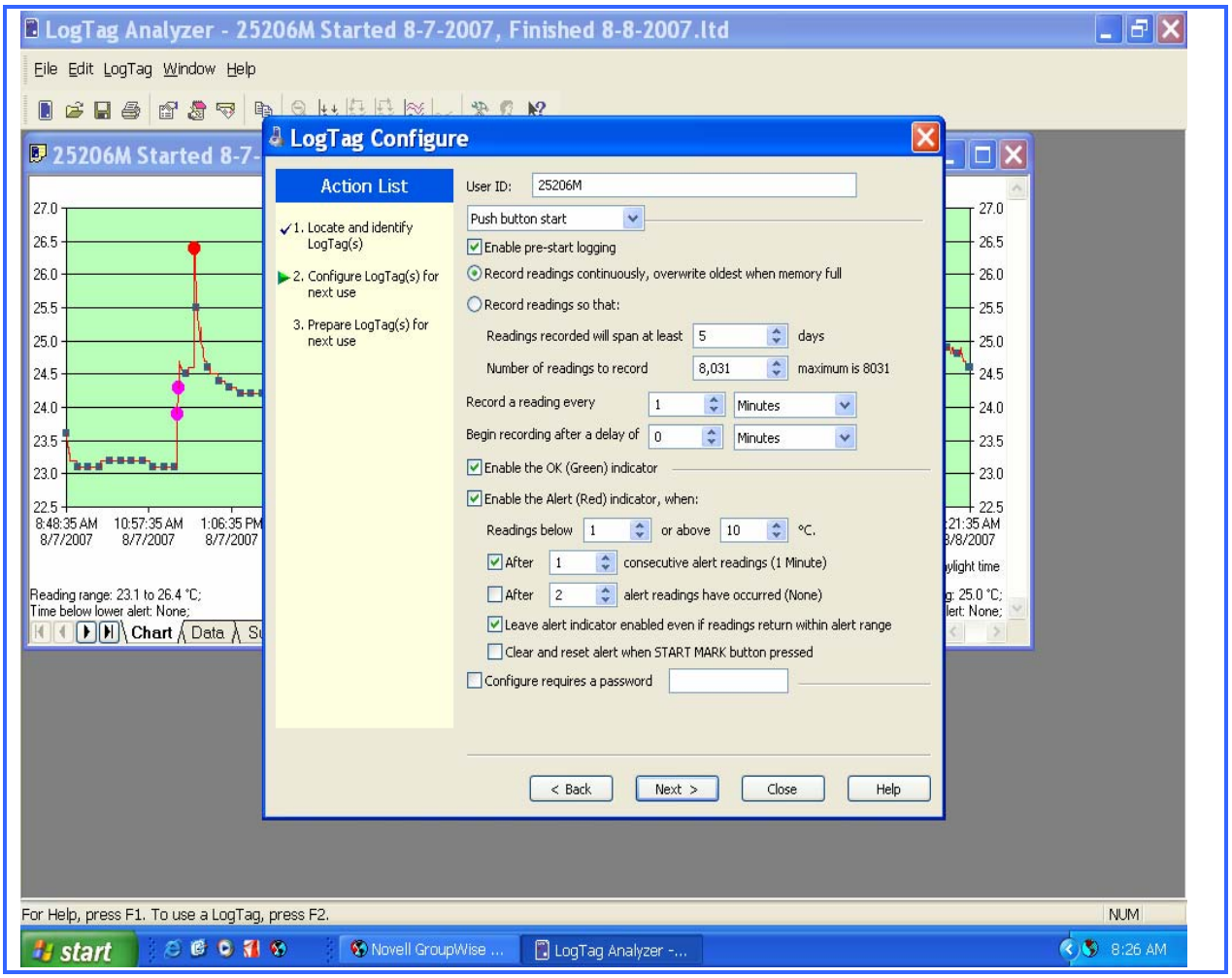
Accurate, continuous temperature data is crucial to validating and monitoring temperature sensitive materials. The Global Sensor product is for chilled and room temperature applications only.

The benefits of the log tag analyzers were:

- Self-contained - no cables running from probes inside the test container
- Provides continuous data
- Easily paired to provide matching payload and ambient readings
- Plug and play simplicity with any PC
- Data is easily extracted to other programs

Note: (For all frozen applications, use another model to temperature monitoring device.)

***Figure 3: Computer graphics of the configuration used for the validation process.***

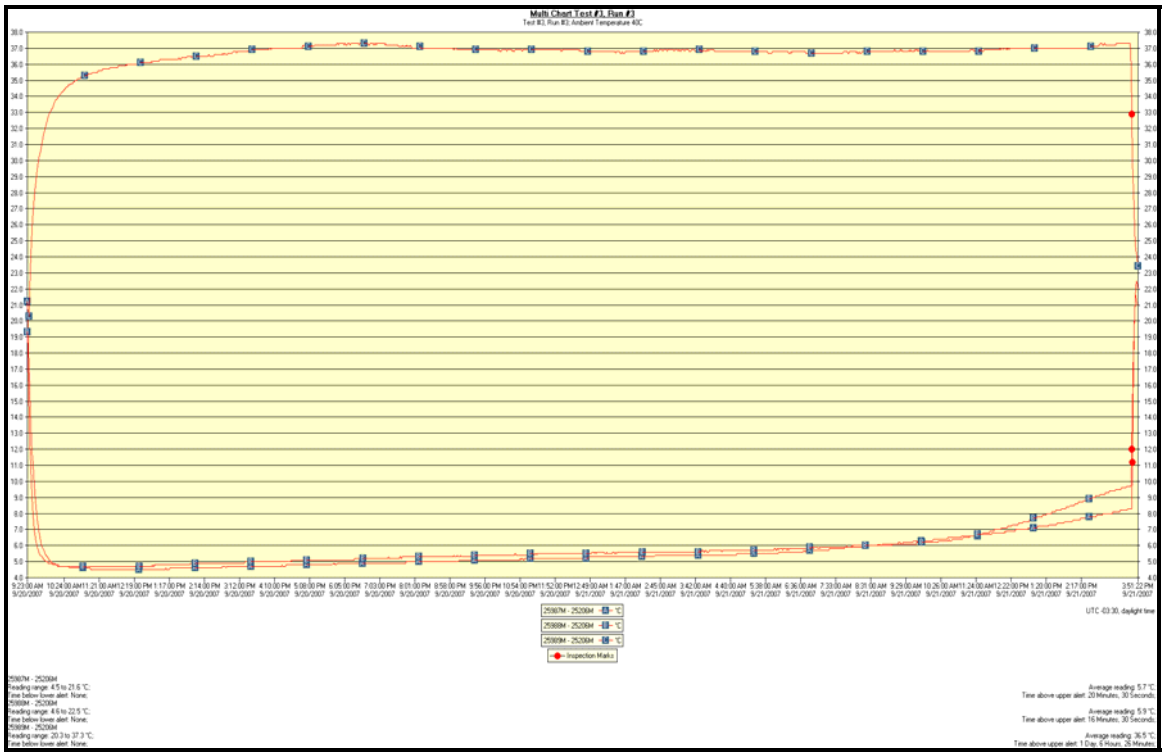


## VALIDATION PROCESS

The validation was carried out over a period of months incorporating various scenarios that were representative of shipping conditions at several temperatures. The Laboratory validation included simulated shipping at selected temperatures ( -20°C, 4°C, 22°C and 40°C), representative of the various temperatures that the shipping containers would be exposed to during packing and awaiting transfer to airports or courier. The results of the validation studies were documented in the validation protocol. Scenarios also included pre-conditioning the containers between 4-6°C as well as at 6°C as many hospital blood bank refrigerators are set between 4-6°C. It was interesting to note that as long as the PCM in the TIC was liquid, the target testing time of thirty hours was met or exceeded. If the TIC was pre-conditioned at a temperature very close to 4°C the target testing time of thirty hours was reduced while the product temperature was maintained between 1°C to10°C.

Below is a sample graph depicting results of 3 log tags; ambient temperature measuring the external temperature during shipping, log tag in the bottom of the shipping container and a log tag placed on the sidewall within the shipping container.

***Figure 4: Sample of a multi-chart graph***



Individual and combined charts were prepared for each test scenario and the results evaluated. The graphics of the combined charts and individual charts were then exported to Excel so that members of the IHTWG could review the data.

Deficiency reports reflect excursions incurred during various test runs. Resolution of the deficiencies was completed prior to beginning the next test phase. Most of these deficiencies were related to documentation errors, rather than failure of the shipping container or the temperature monitoring devices.

Modes of transportation included shipping by air during winter and summer seasons from a northern hospital site in Labrador to more southern site in Newfoundland. This represented the greatest air transit distance that red cells would be shipped within Newfoundland and Labrador. Ground transportation via a commercial courier was also tested. In this scenario, the internal temperature of the courier van was monitored and shipping container was pre-conditioned accordingly.

A survey of the provincial hospitals was conducted to ensure the availability of suitable storage units for pre-conditioning the shipping containers.

## RESULTS

The validation process was completed using various shipping scenarios. Each test run was evaluated and a determination was made regarding whether additional runs were required. Charts were downloaded and summary tables (Tables 1,2,3) were prepared as noted below.

***Table 1: Average Temperatures in Field Validation Tests***

| Summary of Test Runs - Field Validation | | | | | | |
|---|---|---|---|---|---|---|
| | Summer | | Winter | | Ground | |
| | Payload | | Payload | | Payload | |
| | 1 Unit | 4 Units | 1 Unit | 4 units | 1 Unit | 4 units |
| Average Ambient Temp | 15.9 | 15.7 | 8.0 | 7.1 | 14.5 | 14.4 |
| Average Temp On Receipt | 4.4 | 4.0 | 6.7 | 6.6 | 5.0 | 4.9 |
| Average Transit Time | 8.3 | 8.3 | 8.2 | 8.1 | 8.8 | 8.7 |

***Table 2: Overall Average Temperatures in Field Validation Tests***

| Overall Averages - Field Validation | | | |
|---|---|---|---|
| | Air-Summer | Air-Winter | Ground-Summer |
| Average Ambient Temp | 15.8 | 7.6 | 14.5 |
| Average Temp On Receipt | 4.2 | 6.6 | 5.0 |
| Average Transit Time | 8.3 | 8.1 | 8.8 |

*Table 3: Overall Average Temperature in Laboratory Validation Tests*

| Summary of Test Runs - Laboratory Validation | | |
|---|---|---|
| Ambient Temperature | Payload | Payload |
| | 1 RBC Unit | 4 RBC units |
| -20°C | 5.5 | 5.6 |
| 4°C | 5.4 | 6.5 |
| 22°C | 5.0 | 4.7 |
| 40°C | 5.4 | 5.1 |

## CONCLUSION

A review of the data collected demonstrated that the Golden Hour 24/2 Shipping container and the Log Tag Analyzer would effectively meet the need to transfer red blood cells from one hospital to another within the province of Newfoundland and Labrador.

The use of the Log Tag Analyzer during transit would serve to continuously monitor and validate the shipping containers.

Shipping containers and Log Tag Analyzer kits were purchased and distributed to each of the Regional Health Authorities (RHAs) within the province. Additional Log Tag Interfaces were purchased as required to meet regional needs. Training sessions were conducted in three of the RHAs with an anticipated start up date of September, 2008.

A working group of Provincial Blood Coordinating Programs from several sites across Canada supported this initiative. The Ontario Blood Coordinating Network (ORBCON) also conducted field validation tests among a group of hospitals within Northern Ontario. The results obtained from the field validation also concurred with the results obtained from the field validation tests conducted within Newfoundland and Labrador.

Through the collaborative efforts of ORBCON and the Newfoundland and Labrador Provincial Blood Coordinating Program, a presentation will be made at the International Conference of the American Association of Blood Banks in October 2008 in Montreal, Quebec.

## ACKNOWELDGEMENTS

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