

Temperature-Sensitive Labels for Containers of RBCs

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Abstract

Temperature-sensitive labels are adhesive tags that display color changes at preset temperatures. There have been no studies of the suitability of this technology for measuring the temperature of blood components during transportation and storage. We used a digital thermometer to measure temperature in different locations inside containers of RBCs as they were allowed to warm to ambient temperatures following removal from refrigeration. We compared these temperature readings with those of 3 temperature-sensitive labels. These labels are marketed to alert transfusion services if the temperature of blood bags exceeds 10°C, which is the maximum permissible by Food and Drug Administration and American Association of Blood Banks requirements for transporting RBCs. The contents of refrigerated RBC units changed from one homogeneous temperature to a range of temperatures when containers were allowed to warm (undisturbed) to ambient temperatures. Color changes of all 3 temperature-sensitive labels correlated more with core compared with surface temperatures of RBC units. These devices add an additional dimension of safety to the conventional 30-minute rule, which limits storage of blood components at ambient temperature to 30 minutes.

The American Association of Blood Banks and US Food and Drug Administration require human blood or components to be stored at 1°C to 6°C and not to exceed 10°C when transported.¹⁻³ Ensuring compliance is logistically difficult, however, when blood is stored or transported outside the transfusion service's supervision and control. Specialized storage containers have been developed for long-distance or long-term applications.⁴ However, in day-to-day operations, transfusion services typically manage this function according to the 30-minute rule, ie, refrigerated blood components may be held at ambient temperature for no longer than 30 minutes.⁵

In recent years, manufacturers of temperature-sensitive indicators have marketed devices to transfusion services as aids to ensure compliance with requirements for monitoring the temperature of stored and transported blood components. Two types of temperature-sensitive sticky labels are available for transfusion services. *Temperature indicators* monitor whether a component's temperature has exceeded a set value.⁶ *Time-temperature integrators* display time and temperature measurements as a single result.⁶ Although similar devices are used in the food industry,^{7,8} we are not aware of any studies of the suitability of temperature-sensitive labels fixed to the exterior surface of blood containers for monitoring the temperature of blood components outside of temperature-monitored refrigeration. We conducted the present study to evaluate the contribution that temperature-sensitive labels might make to safe transportation and storage of refrigerated blood components.

Materials and Methods

Temperature-Sensitive Labels

We evaluated 2 temperature indicators (Check-Spot, Harald H. Temmel KEG, Gleisdorf, Austria; and Safe-T-Vue, William Laboratories, Enfield, CT) and 1 time-temperature integrator (HemoTemp II Indicator, Biosynergy, Elk Grove Village, IL).

Check-Spot is a self-adhesive label with an integrated temperature indicator supplied on rolls. Check-Spot is manufactured using proprietary phase change technology with paraffin compounds (crystalline alkyl hydrocarbons), which change from solid to liquid and then to vapor. The materials are formulated to melt at a designated temperature, which is displayed by a color change from white to red. This temperature indicator is activated when fixed on the surface of the blood bag. Check-Spot is preconditioned by storage at 1°C to 6°C for 1 hour, activated, and applied to the blood bag using a manufacturer-supplied mechanical device (Spot-Gun, Harald H. Temmel KEG). According to the manufacturer, the indicator has been calibrated to begin to change from white to finally dark red when the blood bag core temperature reaches 9.6°C. At 10.4°C, color change ceases and is irreversible. Accuracy, according to the manufacturer, is $\pm 0.5^\circ\text{C}$. Beside the integrated activation display (green) a “DON’T TOUCH” warning is printed on the label to prevent accidental warming by human contact.

Safe-T-Vue also is manufactured using proprietary technology. The manufacturer’s instructions are to refrigerate the label for at least 24 hours before use and attach it to the blood bag where there is the greatest volume of blood. Each label must be prepared individually by peeling a “remove” sticker, placing it on a blood bag, peeling a top foil lid, and snapping 2 round parts together, which comprise the label. A white center indicates a safe temperature ($<10^\circ\text{C}$). A change to red in the center of the indicator is intended to reflect when the core temperature approaches 10°C .

HemoTemp II contains an irreversible liquid crystal time-temperature integrator and a reversible liquid crystal thermometer. This time-temperature integrator has been calibrated to change from blue to green when the core temperature of the blood unit is approximately 10°C . The color continues to change irreversibly to tan and, finally, to brown. According to the manufacturer, the starting temperature of the bag must be between 1°C and 4°C. We measured the core temperature of each bag and ensured the temperature was 4°C or less. Before applying the label, it must be heated to 37°C to 40°C for 60 seconds or longer and removed from the heat source; an irreversible “flower” begins to appear. When the flower turns blue, the backing is removed and the indicator pressed onto the center or near the bottom of a refrigerated

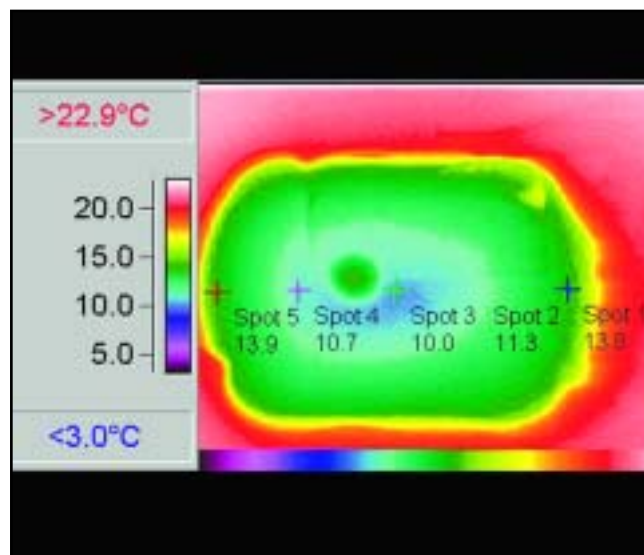
blood bag (1°C–4°C). After activation, the irreversible indicator remains blue for at least 72 hours if the blood is stored at 4°C. When the internal temperature of the blood bag is approximately $10^\circ\text{C} \pm 0.5^\circ\text{C}$, the indicator loses the blue color and will not return to blue, even if the blood bag is cooled.

Red Blood Cells

For the study, we obtained recently outdated adenine-saline added) or citrate-phosphate-dextrose-adenine units of RBCs that had been supplied to the hospital by the American Red Cross Blood Services. The adenine-saline added units were prepared by centrifugation of whole blood, removal of plasma, and resuspension of the RBCs in 100 to 110 mL of a dextrose, adenine, sodium chloride, and mannitol solution. The final component had a hematocrit of 55% to 65% (0.55–0.65) and a total volume of 300 to 400 mL. The citrate-phosphate-dextrose-adenine units of RBCs were prepared by collecting whole blood in an anticoagulant solution consisting of citrate, phosphate, dextrose, and adenine and centrifuging the mixture to remove sufficient plasma for a final hematocrit of 65% to 80% (0.65–0.50) and a total volume of approximately 225 to 350 mL.

Measuring Temperatures With the Digital Thermometer

Preliminary studies using a thermographic camera provided *indirect* evidence of variations in the temperature of contents of refrigerated units of RBCs that had been removed and allowed to warm at ambient temperature ■Image 1■. Based



■Image 1■ Temperature recordings by a thermographic camera of a blood bag removed from refrigerated storage (2°C–6°C) and placed at room temperature (25°C) for 33 minutes (Courtesy of Jakob Woisetschläger, PhD, Graz University of Technology, Graz, Austria). The image reflects variations in temperature at different locations of a blood bag as the contents warmed from refrigerated to ambient temperature.

on these findings, we developed a protocol for *direct* measurement of the contents of such units of RBCs, selecting sites within the bags that represented the lowest temperatures (central “core” locations) and the warmer temperatures (peripheral locations).

We measured the temperatures of blood components using a Traceable Big Digit Memory Thermometer (Control Company, Houston, TX). The thermometer was calibrated using instruments traceable to the National Institute of Standards and Technology (NIST). The thermometer’s probe ranges were -50°C to 70°C . Resolution was 0.1°C . We read temperatures after a sampling time of at least 10 seconds.

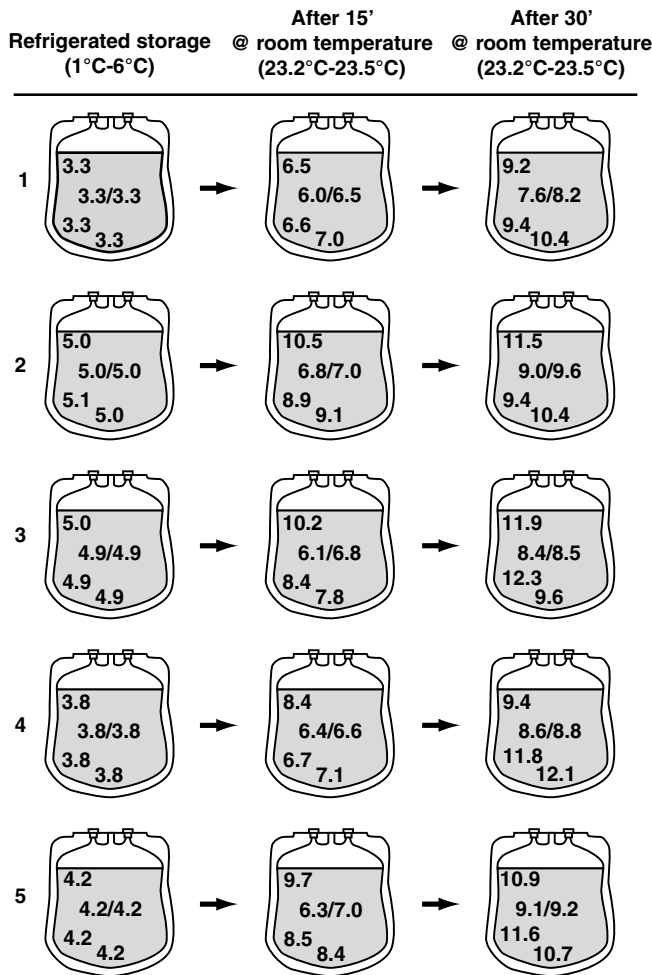


Figure 1 Digital thermometer temperature measurements of the contents of 5 U of RBCs. Temperatures were measured during refrigerated storage (1°C - 6°C) at 5 locations inside the blood bags: a top corner, core/center surface, bottom midline, and a bottom corner. The digital thermometer measurements were repeated at the same locations after the bags had been removed from refrigerated storage and maintained at ambient room temperature (23.2°C - 23.5°C) for 15 and 30 minutes.

According to the manufacturer, the external probe monitored temperatures in air, gas, liquids, and semisolids with an accuracy of $\pm 1^{\circ}\text{C}$.

By using the NIST-calibrated digital thermometer, we measured blood temperature at 5 specific locations inside a vertically placed unit of RBCs: a top corner, center-center (core), center surface, a bottom corner, and bottom midline (Figure 1). Because the units of RBCs were positioned vertically, “center” refers to the central (coldest) location of the unit’s contents. This location was slightly below the true center position of the bag. The probe was inserted via a hole cut adjacent to the blood bag’s administration port. We recorded temperatures at these locations after 24 hours of refrigerated storage (1°C - 4°C) and at 15 minutes and 30 minutes at ambient temperature (23.2°C - 23.5°C) following their removal from the refrigerator.

Digital Thermometer vs Temperature-Sensitive Labels

To evaluate performance of the temperature-sensitive labels, we compared digital temperature readings at each of the 5 internal locations with readings of the 3 temperature-sensitive labels applied according to manufacturers’ instructions to the external surface of the blood containers. We compared these temperature readings for 10 units of RBCs and evaluated the temperature-sensitive labels for accuracy, repeatability (precision), and irreversibility.

To evaluate accuracy, we compared visual alerts of the 3 types of temperature indicators with NIST-calibrated thermometer readings when the containers were removed from refrigerated storage and placed in ambient temperature. We recorded the times and core temperatures at which the irreversible portions of the labels began to change color (Figure 2). For repeatability (precision), we repeated measurements with 10 of the 3 indicators using 10 different units of recently outdated RBCs (Figure 2). To ensure that the temperature indicators had undergone an irreversible change and did not revert after activation, we attached 3 indicators to 8 containers of RBCs, removed from them from the refrigerator, allowed the color to change irreversibly, returned the bags to a 3°C to 4°C refrigerator and observed for color changes after 30 and 60 minutes.

Results

Temperature Changes Inside Containers of RBCs

Digital thermometer temperature measurements of the contents of refrigerated units of RBCs (1°C - 6°C) showed minimal variations between core and peripheral locations (Figure 1). However, after the blood bags were removed from the refrigerator, temperatures warmed more quickly at the peripheral locations than at the core. After 15 minutes at ambient temperature, we observed discrepancies between temperatures in

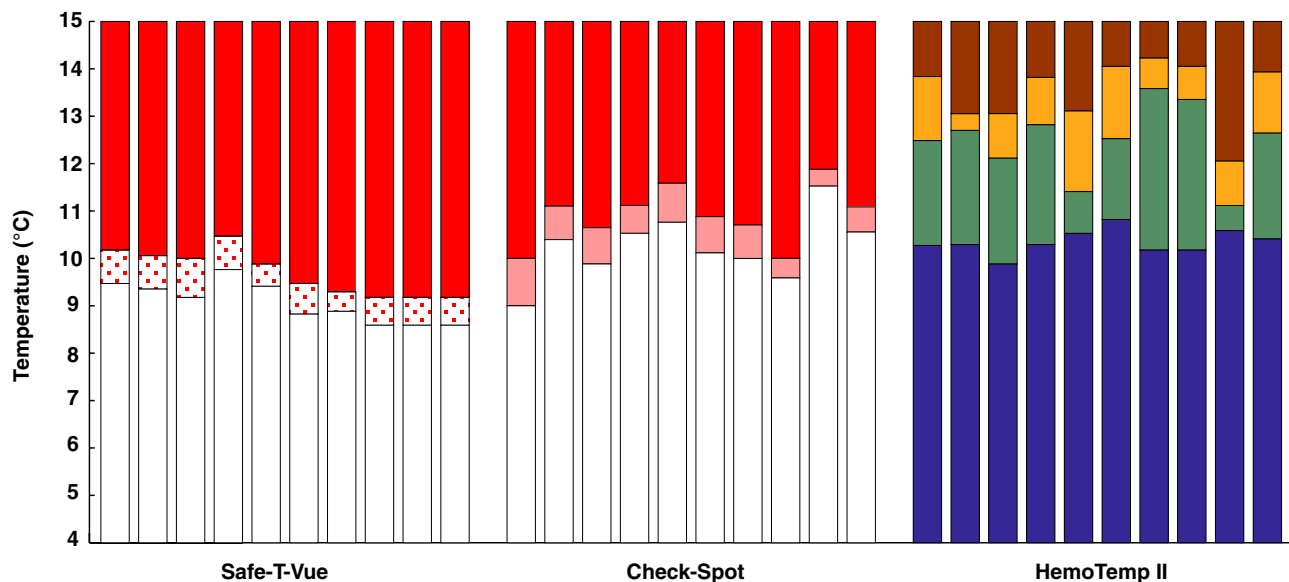


Figure 2 Color changes of temperature-sensitive labels after units of RBCs were removed from refrigerated storage (1°C–6°C) and allowed to warm to 15°C while stored at ambient room temperature (20.2°C–25.1°C). For Safe-T-Vue (n = 10), the first color changes were observed when red dots appeared on the labels between 8.6°C and 9.8°C. The final color change, a solid red, occurred between 9.2°C and 10.4°C. For Check-Spot (n = 10), the first color changes were observed when labels turned pink between 9.0°C and 11.5°C. The final color change, solid dark red, occurred between 10°C and 11.9°C. For HemoTemp II (n = 10), the first color changes were observed when labels turned from blue to green between 9.9°C and 10.7°C. The labels changed from green to tan between 11.2°C and 13.6°C and, finally, to brown between 13.1°C and 14.3°C.

peripheral locations compared with the core. After 30 minutes, none of the temperatures in peripheral locations reflected the core temperature of the contents of the containers of RBCs (Figure 1).

The Safe-T-Vue temperature indicators turned from white to red dots at $9.1^{\circ}\text{C} \pm 0.4^{\circ}\text{C}$ and to red at $9.7^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$ (Figure 2). Safe-T-Vue labels were easy to apply. Assessment of the occurrence of a color change was clear and unambiguous.

Check-Spot temperature indicators changed from white to pink at $10.2^{\circ}\text{C} \pm 0.7^{\circ}\text{C}$ and to red at $10.9^{\circ}\text{C} \pm 0.6^{\circ}\text{C}$ (Figure 2). Check-Spot, combined with the activator Spot-Gun, was easy to handle. We observed some variation in the intensity of the color change from production lot to lot, but readings were clear and unambiguous.

The HemoTemp II time-temperature integrators changed from light blue to green at $10.3^{\circ}\text{C} \pm 0.2^{\circ}\text{C}$, to tan at $12.5^{\circ}\text{C} \pm 0.7^{\circ}\text{C}$, and to brown at $13.6^{\circ}\text{C} \pm 0.7^{\circ}\text{C}$ (Figure 2). HemoTemp II labels were easy to apply. Observers required practice to interpret the color changes reliably.

All temperature-sensitive labels maintained irreversible color changes when returned to 3°C to 4°C and checked for color at 15 minutes and 1 hour. We tested 8 of each manufacturers' temperature-sensitive labels. All labels remained firmly in place during the study, provided they were adhered to a thoroughly dry surface on the blood container.

Discussion

To our knowledge, this is the first study that directly measured temperatures in different locations inside containers of RBCs as they warmed to ambient temperatures after removal from refrigerated storage. By comparing these temperature readings with those of temperature-sensitive labels on the external surface of containers of RBCs, we were able to make the following observations about their suitability as safety devices for transfusion services:

First, as illustrated by the thermographic image, the contents of refrigerated RBCs changed from one homogeneous temperature to a range of temperatures, if allowed to warm (undisturbed) to ambient temperatures. Not unexpectedly, temperatures of the contents of a container of RBCs remained relatively cool at the interior core for several minutes, whereas temperatures near the surface began to increase within a few minutes toward ambient temperatures. Thus, *one* temperature-sensitive label fixed to *one* external location on a container can provide general information but cannot capture the calculus (rate of change) or geometry (different locations) of temperatures inside a container of RBCs.

Second, despite these limitations, we found that all 3 temperature-sensitive labels satisfactorily reflected the temperature of the major proportion (core) of the contents of the container.

As technical devices, the labels were precise. Any limitations of temperature-sensitive labels for this application in transfusion services is more likely to be due to variations in temperature of the contents of blood containers rather than with the devices' technical capability for measuring temperature at a specific site.

Last, we conclude that these devices offer transfusion services an opportunity to develop and validate their own in-house procedures to supplement and, thereby, improve on decisions using the 30-minute rule. For example, if a unit of RBCs were overheated by placement on a hot surface (eg, microwave heater, radiator, or the top of a refrigerator) but returned within 30 minutes to the transfusion service, its potential unsuitability would not be identified by a transfusion service relying only on the 30-minute rule. However, such a potentially unsuitable unit would be likely to be recognized if a temperature-sensitive label had been in place.

Also, procedures can be developed to use temperature-sensitive labels to avoid unnecessary and costly discards of blood components when storage for more than 30 minutes outside a temperature-monitored refrigerator raises questions about suitability. In our hospital, we require RBCs to be returned to the transfusion service if the transfusion cannot be started within 30 minutes. Routinely, we attach a temperature-sensitive indicator to the container before we issue the unit of RBCs from the transfusion service. If a unit of RBCs is returned untransfused after more than 30 minutes but the temperature has not reached 10°C according to the temperature-sensitive indicator, we do not discard the unit. The findings of the present study provide guidance for other transfusion services to evaluate and validate the suitability of temperature-sensitive labels for their specific needs and applications to increase transfusion safety and avoid unnecessary wastage.

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