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Validation of the Cold Chain Product (CCP) delivery process for whole blood

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ABSTRACT

Background: Donor blood is obtained through mobile blood donation activities and fixed Blood Transfusion Units in Jakarta Province and subsequently transported to the Blood Processing Unit using insulated containers (cool boxes). Maintaining an uninterrupted cold chain during transportation is essential to preserving blood quality. One critical factor influencing temperature stability is the proportion between blood bags and ice packs within the transport container. This study aimed to validate the Whole Blood Cold Chain Product (CCP) transportation process by determining an optimal blood bag-to-ice pack ratio capable of maintaining the required temperature range during delivery.

Methods: Validation was performed sequentially through three stages: design validation, operational validation, and performance validation. Each stage was evaluated against predefined acceptance criteria, with validation outcomes determined by comparing observed results to these criteria before proceeding to subsequent stages.

Results: Design validation confirmed that the cool box and ice pack specifications met established acceptance requirements. During operational validation, dummy blood bags were arranged with varying numbers of ice packs and exposed to three different ambient temperature conditions. Temperature measurements from the dummy bags consistently fulfilled acceptance criteria. Performance validation, conducted using actual Whole Blood units under two ambient temperature conditions, demonstrated that blood bag temperatures remained within the acceptable range when packed according to validated ratios.

Conclusion: The study confirms that specific packing configurations and ratios of blood bags to ice packs can be effectively applied to ensure controlled and reliable transportation of Whole Blood Cold Chain Products.

Keywords: Cold Chain Product, Cool Box, Design Validation, Operational Validation, Performance Validation

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INTRODUCTION

Donor blood collection is conducted through mobile blood donation units and fixed Blood Transfusion Units operated by the Indonesian Red Cross in Jakarta. Blood donation activities generally last 3–4 hours, followed by transportation to the Blood Processing Unit, which may take an additional 1–2 hours. Considering that ambient temperatures in Jakarta frequently reach 35–40 °C, appropriate containers and handling procedures are required to maintain blood quality during transportation.¹

Whole blood is classified as a cold chain product, indicating that its temperature must be consistently controlled from the time of collection until transfusion to the patient. Maintaining blood within the recommended temperature range is essential to prevent cellular damage, metabolic deterioration, and

hemolysis during transport, which may compromise transfusion safety and efficacy.^{1,2} Temperature control during transportation is commonly achieved using insulated containers (cool boxes) combined with cooling elements such as ice packs. However, stable thermal conditions are not solely dependent on the presence of cooling materials but also on the appropriate ratio and arrangement of blood bags and ice packs within the container. Improper packing configurations may result in temperature deviations that jeopardize blood integrity.^{2,3}

Therefore, validation of the blood transportation process is necessary to ensure that the selected cool box system, ice pack type, packing configuration, environmental temperature, and transport duration can consistently maintain the required temperature range.

International guidelines emphasize that transport containers for blood and blood components must be durable, validated, and capable of preserving specified storage conditions throughout the expected transport period. Validation provides objective evidence that the cold chain is maintained in accordance with quality and safety standards for blood products.^{1,4,5} Based on those mentioned above, this study aims to evaluate the validation of the Cold Chain Product (CCP) delivery process for whole blood.

METHODS

The validation process was conducted sequentially in three stages: design validation, operational validation, and performance validation, in accordance with PIC/S guidelines.⁶ Predefined acceptance criteria governed each validation stage, and

progression to the subsequent stage was permitted only if these criteria were met. Validation outcomes were determined by systematically comparing observational results with the established acceptance criteria at each stage. The validation process was considered successful only when all stages fulfilled their respective acceptance requirements.

Design validation was initiated after confirming the availability of prerequisite documentation, including equipment acceptance records and detailed specifications of the cool box. If these prerequisites were satisfied, design qualification was performed; otherwise, design validation could not proceed. Design validation of the cool box involved assessment of seven parameters: empty weight, dimensions, tie rod/handle integrity, capacity, mobility, presence of a drainage outlet, and the condition of the internal surface. Ice packs were evaluated based on two parameters: size and type. When all acceptance criteria were met, the validation process advanced to operational validation. If deviations were identified, confirmation with the supplier and re-inspection were conducted when necessary. Deviations that did not affect the performance or function of critical components were documented and justified in the validation report, allowing progression to the next stage. However, if non-conformities were found to compromise critical functionality, validation was discontinued, and the process was deemed unsuitable for implementation.

Operational validation was performed only after successful completion of design validation. The required prerequisites included the validated cool box, internal dividers (hollow boards), ice packs, dummy blood bags, and trained personnel. Operational validation was conducted under three different ambient temperature conditions ranging from 22°C to 30°C, reflecting environmental conditions during blood donation activities and transportation in air-conditioned vehicles. The placement of dummy bags and ice packs within the cool box is illustrated in Figure 1, while the corresponding ratios are presented in Table 1.

At ambient temperatures of 22–24°C, operational validation began with a precooling phase in which 10 ice packs were placed inside the cool box for 1 hour. Subsequently, the ice packs were temporarily removed, leaving two ice packs in the container, after which six dummy bags were added. Every 10–20 minutes, two ice packs and six dummy bags were incrementally reintroduced until a total of 30 dummy bags and 10 ice packs were reached (Figure 2). For ambient temperatures of 25–27°C, the precooling phase involved 12–13 ice packs for 1 hour, followed by the same incremental loading procedure until 30 dummy bags and 12–13 ice packs were achieved. At ambient temperatures of 28–30°C, precooling was conducted using 15 ice packs for 1 hour, with subsequent staged loading until 30 dummy bags and 15 ice packs were placed in the cool box.

Acceptance criteria for operational validation required that dummy bag temperatures remained within 20–24°C, with a tolerance of less than 1°C below the upper limit (maximum 24.9°C), and a minimum compliance rate of 75%. If acceptance criteria were not met, confirmation with the supplier and re-evaluation were undertaken when necessary. Deviations that did not affect critical performance were justified in the validation report, allowing progression to performance validation. However, deviations affecting critical functionality resulted in termination of the validation process.

Performance validation was conducted following successful operational validation. Prerequisites included the validated cool box, internal dividers, ice packs, trained personnel, and actual Whole Blood units. Performance validation was carried out during mobile blood donation activities

using procedures identical to those applied in operational validation, with dummy bags replaced by Whole Blood bags. When all acceptance criteria were satisfied, validation using Whole Blood was deemed successful. If acceptance criteria were not met, root cause analysis was performed and corrective actions, including repeat testing, were undertaken.

RESULTS

Prior to initiating design validation, several prerequisite conditions had to be fulfilled, including the availability of equipment acceptance documentation and detailed technical specifications of the cool box. Based on the initial assessment, all prerequisite requirements met the established acceptance criteria, thereby allowing the design validation process to proceed. Design validation of the cool box involved evaluation of seven parameters: empty weight, dimensions, tie rod/handle integrity, storage capacity, mobility, presence of a drainage outlet, and the condition of the internal surface. In addition, ice packs were assessed according to two parameters, namely size and type. Observational findings demonstrated that all evaluated parameters complied with the predefined acceptance criteria. Consequently, the design validation stage was considered successful, and the process was permitted to advance to the operational validation phase.

The operational validation prerequisites that must be fulfilled prior to conducting operational validation included successful completion of design validation, availability of partition boards (hollow boards) matching the cool box dimensions, and the presence of dummy bags and ice packs that had been frozen for a minimum of 12 hours in a freezer. All operational validation prerequisites

Table 1. Comparison of ice packed with bags/dummy bags

No	Model	Room Temperature (°C)	Blood count (Bag)	Quantity Ice packed (Number)	Number and position of Ice packed			
					Down (A)	Back (B)	Centre (C)	Up (D)
1	Type 1	22-24	30	10	3	1	3	3
2	Type 2	25-27	30	12-13	3	1	4	4-5
3	Type 3	28-30	30	15	3	1	5	6

met the acceptance criteria; therefore, the operational validation process could be initiated. Operational validation was performed by sequentially placing dummy bags and ice packs at room temperature under three environmental models: Type 1 (22–24 °C), Type 2 (25–27 °C), and Type 3 (28–30 °C), as outlined in Table 1. Based on observations, the operational validation results across all three-room temperature conditions met the acceptance criteria, with dummy bag temperatures consistently maintained within the range of 20–24 °C. The acceptance rate achieved was 100%, indicating that operational validation was successfully passed and the process could proceed to performance validation (Table 2 and Table 3).

Operational validation is declared passed, followed by performance validation. The prerequisite for performance validation is that operational validation is declared passed, and Hallow boards are available according to the size of the cool box, whole blood bag, and ice pack that have been frozen for at least 12 hours in the freezer. All performance validation prerequisites have met the acceptance criteria so that the performance validation process can be carried out. Performance validation was carried out in unit car activities and was carried out only at room temperature types 1 (22–240 °C) and 2 (25– 270 °C), because there were no unit car activities at type 3 room temperature (28– 300 °C). The performance validation process is carried out by placing blood bags and ice packs gradually at room temperature for type 1 and type 2 models according to Table 1. Based on observations, the results of performance validation at room temperature type 1 (22–240C) were according to the acceptance criteria with each blood temperature ranging from 20–240C with an acceptance value of 100% and the results of performance validation at room temperature type 2 (25–270C) according to the acceptance criteria with a temperature of 29 blood bags ranging from 20–240C and one blood bag temperature of 26.80C with an acceptance value of 97% (75% acceptance criteria). Based on the results of the validation, the performance validation process was declared passed (Table 4 and Table 5).

Table 2. Prerequisite Activities

No	Activities	Acceptance Criteria	Observations	Results
1	Operational Validation	Operational validation can be carried out if the design validation test is declared passed	Design validation is declared passed, so that it can proceed to operational validation	
2	Hallow board	Hallow board according to the size of the cool box	A set of 4 Hallow boards is available	Meet the acceptance criteria
3	Ice packed	Has been frozen for min 12 hours in the freezer	Ice packed has been frozen for 12 hours	
4	Dummy bag	Temperature of 25–28°C	30 dummy bags available	

Table 3. Operational Validation Checklist

Parameter	Test Procedural	Acceptance Criteria	Concordance of Results
Room temperature 22–24°C	Put dummy bags and ice packed gradually with type 1 models	The temperature of each bag ranges from 20–24°C, with a target of achieving a minimum of 75%	Meet the acceptance criteria
Room temperature 25–27°C	Gradually place dummy bags and ice packs with type 2 models		
Room temperature 28–30°C	Gradually place dummy bags and ice packs with type 3 models		

Table 4. Prerequisite Activities

No	Activities	Acceptance Criteria	Observations	Results
1	Performa Validation	Performance validation can be carried out if the operational validation test is declared passed	Operational validation is declared passed, so that it can proceed to performance validation	Meet the acceptance criteria
2	Hallow board	Hallow board according to the size of the cool box	A set of 4 Hallow boards is available	
3	Ice packed	Has been frozen for min 12 hours in the freezer	Ice packed has been frozen for 12 hours	
4	Blood bag	Whole blood products	Available	

Table 5. Performance Validation Checklist

Parameter	Test Procedural	Acceptance Criteria	Concordance of Results
Room temperature 22–24°C	Gradually place blood bags and ice packed with type 1 models	The temperature of each bag ranges from 20–24°C with a target of achieving a min of 75%	Meet the acceptance criteria
Room temperature 25–27°C	Gradually place blood bags and ice packed with type 2 models		

DISCUSSION

From the moment blood is collected from a donor, strict maintenance of the cold chain is essential to preserve blood quality, as whole blood is classified as a Cold Chain Product (CCP). Temperature deviations during storage or transportation accelerate cellular metabolism, increase membrane fragility, and promote hemolysis, ultimately compromising transfusion safety and clinical effectiveness. Experimental and observational studies have consistently shown that exposure of whole blood to suboptimal temperatures leads to biochemical deterioration and reduced red blood cell (RBC) viability.^{7,8}

Indonesian national regulations mandate that blood and blood components be transported under controlled temperature conditions to ensure quality and patient safety. This requirement is consistent with international transfusion medicine standards, which emphasize that blood transport systems must be validated to demonstrate their ability to maintain defined temperature ranges for the expected duration of transport. Validation is therefore not merely administrative but a core component of quality assurance in blood establishments.⁹⁻¹¹

International guidelines further specify that transport containers must be physically robust, resistant to leakage and contamination, and designed to allow effective cleaning and disinfection between uses. The World Health Organization (WHO) recommends insulated containers with sufficient thermal mass to withstand environmental temperature fluctuations, particularly in tropical climates. However, these guidelines also acknowledge that local resource constraints may necessitate the use of alternative containers, provided that formal validation demonstrates adequate thermal performance.^{10,12}

In the present study, validation was conducted because the available Igloo® cool boxes at the Blood Transfusion Unit of the Indonesian Red Cross Society in Jakarta have an insulation thickness (2–3 cm) below the WHO-recommended specification. Previous studies have demonstrated that container performance is determined not solely by insulation thickness but also by packing configuration, ice pack ratio, and airflow

restriction within the container. Sharley et al. showed that validated transport systems using non-ideal containers could still reliably maintain blood temperature during aeromedical retrieval when appropriate design and packing strategies were applied.³

The validation results demonstrated that cold chain integrity could be maintained across three ambient temperature ranges (22–30°C) by adjusting the number of ice packs relative to the blood load. Blood or dummy bag temperatures remained within the acceptable range of 20–24°C using 10 ice packs at 22–24°C, 12–13 ice packs at 25–27°C, and 15 ice packs at 28–30°C. These findings align with previous experimental data showing that ice-to-blood ratios are a dominant determinant of thermal stability during transport, often outweighing container insulation thickness alone.^{4,13}

Despite these favorable findings, several limitations must be acknowledged. Validation was not performed at ambient temperatures exceeding 30°C, which are frequently encountered in tropical urban environments. In addition, the validated transport duration was limited to 3 hours, whereas longer transport times may occur during extended mobile donation activities. Furthermore, this study did not include post-transport laboratory quality assessments such as hemolysis index, RBC morphology, or lactate dehydrogenase (LDH) levels. Prior studies have demonstrated that temperature deviations during transport are directly associated with increased hemolysis and biochemical markers of RBC damage, underscoring the importance of incorporating quality testing into future validation protocols.^{4,14} Future validation studies should therefore include higher ambient temperature scenarios (>30°C), longer transport durations, and dynamic conditions such as vehicle movement and intermittent container opening. Most importantly, validation should be extended beyond temperature monitoring to include objective laboratory indicators of blood quality, ensuring that validated transport conditions preserve not only thermal stability but also cellular integrity and transfusion efficacy.^{14,15}

CONCLUSION

Based on the validation results, it can be concluded that specific packing configurations and defined ratios between whole blood bags and ice packs can be effectively implemented to ensure controlled transportation of Whole Blood Cold Chain Products (CCP). The validated packing method was able to maintain the required temperature range throughout the transportation process under the tested environmental conditions, thereby supporting cold chain integrity and contributing to the preservation of blood quality during delivery.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest associated with this study.

FUNDING

This study did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

ETHICS CONSIDERATION

This study involved a validation process of blood transportation systems and did not include interventions on human subjects beyond standard blood donation procedures. All activities were conducted in accordance with national regulations and institutional policies governing blood transfusion services. The study complied with ethical principles related to safety, confidentiality, and quality assurance, and did not require individual informed consent as no additional procedures were performed on donors.

AUTHOR CONTRIBUTIONS

RA conceptualized the study, designed the validation protocol, conducted data collection, and drafted the manuscript. N contributed to the operational and performance validation processes and data acquisition. SM participated in data analysis and interpretation. NKR critically reviewed the manuscript and provided scientific input. All authors reviewed and approved the final version of the manuscript.

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