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## Evaluation of Mirasol Pathogen Reduction Technology and its Effects on Platelet Viability and Plasma Integrity in Blood Units

Grace Dado<sup>1</sup>, Dr. Carina M. Magtibay<sup>2</sup>, Lolita C. Aristo<sup>1</sup>, Namshad Parappurath<sup>1</sup>, Dr. Emad Elmagboul<sup>1</sup>, Dr. Godwin Wilson<sup>1</sup>, Dr. Sanjay Doiphode<sup>1</sup>

<sup>1</sup>Hamad General Hospital-Doha, Qatar <sup>2</sup>Lyceum of the Philippines University-Batangas

Corresponding Author: [gpdado315@gmail.com](mailto:gpdado315@gmail.com)

### Abstract

Bacterial contamination of platelet components remains a persistent transfusion safety risk because platelets are stored at room temperature, creating conditions that can permit bacterial proliferation. This study evaluated the effects of riboflavin/ultraviolet-based Mirasol Pathogen Reduction Technology on bacterial suppression in platelet concentrates and on key in vitro indicators of platelet and plasma quality. An in vitro experimental design was employed using 10 pooled platelet concentrate samples prepared in platelet additive solution and 10 single-unit plasma samples. Platelet pools were inoculated with methicillin-resistant *Staphylococcus aureus* and treated using the Mirasol system, with platelet pH and platelet count measured at baseline and during storage (Day 0, Day 3, and Day 7); bacterial persistence was assessed through automated culture monitoring. Plasma units underwent Mirasol treatment with coagulation screening tests (prothrombin time, activated partial thromboplastin time, and fibrinogen) measured pre-treatment, immediately post-treatment, and after 30 days of frozen storage. Repeated measures analysis of variance was applied to evaluate within-unit changes over time. By Day 7, cultures were negative in 9 of 10 treated platelet pools while positive controls remained culture-positive, indicating substantial bacterial suppression under the study conditions. Platelet pH and platelet count declined significantly across storage time points, and plasma testing demonstrated increased clotting times with a marked reduction in fibrinogen following treatment that persisted after frozen storage. Findings support in vitro bacterial suppression with measurable component-quality trade-offs, warranting confirmation using broader microbial challenges and platelet functional and clinical-effectiveness endpoints.

**Keywords:** *Mirasol Pathogen Reduction Technology; pathogen reduction; platelets; plasma; methicillin-resistant Staphylococcus aureus (MRSA); bacterial contamination; platelet storage lesion; platelet pH; platelet count; blood safety; prothrombin time (PT); activated partial thromboplastin time (aPTT); fibrinogen*

### 1. Introduction

Blood transfusion remains an indispensable, life-preserving intervention, yet it carries a persistent safety burden associated with transfusion-transmitted infections. Even with rigorous donor selection and increasingly sensitive screening platforms, residual risk persists because some infectious agents may be below detection thresholds during early phases of infection, and because contamination can be introduced or amplified at multiple points across collection, processing, and storage. Among the recognized transfusion risks, transfusion-transmitted bacterial infection is of particular concern because it can progress rapidly and is strongly associated with severe adverse outcomes. Platelet components warrant heightened attention within this risk landscape because they are

commonly stored at room temperature, a condition that supports bacterial proliferation and therefore increases the likelihood that clinically consequential bacterial loads may develop during the storage window.

To mitigate bacterial contamination, blood services and hospital transfusion programs have implemented layered interventions spanning donor and procedure controls (e.g., donor screening, optimized skin disinfection, diversion pouches), and product-level safeguards (e.g., bacterial detection protocols, leukoreduction, and additive solutions). These measures have reduced bacterial risk but do not eliminate it. Operational constraints—such as delayed bacterial outgrowth, sampling limitations, and system-level variability in contamination sources—create a practical impetus to adopt approaches that target pathogens within the product



itself, rather than relying exclusively on upstream screening or downstream detection.

Pathogen reduction technologies (PRTs) represent a class of product-centered safeguards designed to reduce transfusion-transmitted pathogen risk in labile blood components. Mirasol Pathogen Reduction Technology (MPRT), which employs riboflavin combined with ultraviolet light exposure, is one of the principal PRT platforms used for platelets and plasma. In implementation decisions, however, pathogen reduction efficacy is only one side of the adoption calculus. Blood banks must also contend with whether treatment meaningfully alters platelet storage lesion dynamics (as reflected in measurable storage indicators) and whether plasma remains sufficiently potent with respect to coagulation parameters after treatment and subsequent storage. This unresolved benefit–trade-off profile is precisely the decision-relevant gap that requires more explicit, analytically grounded characterization; further, positioning MPRT relative to other PRT platforms (e.g., Intercept, Theraflex) is necessary to clarify why the specific mechanism and workflow implications of MPRT matter in practice.

Accordingly, the study aimed to evaluate Mirasol pathogen reduction in platelet and plasma components using an *in vitro* experimental model that jointly examines pathogen suppression and component-quality change. Specifically, it assessed whether MPRT-treated platelet concentrates demonstrate bacterial suppression following a standardized bacterial challenge and incubation period; examined changes in platelet storage indicators (pH and platelet count) across defined storage time points (Day 0, Day 3, and Day 7); and determined changes in plasma coagulation screening parameters (prothrombin time, activated partial thromboplastin time, and fibrinogen) measured before treatment, immediately after treatment, and after 30 days of frozen storage. These outcomes were evaluated using repeated measures analysis of variance to quantify within-unit change over time under the study conditions.

## 2. Review of Related Literature

### 2.1 Residual Bacterial Risk in Platelet Transfusion

Platelet concentrates stored at room temperature (RT; 20–24°C) represent a unique and persistent challenge in transfusion safety, carrying a materially higher residual risk of transfusion-transmitted bacterial infection (TTBI) compared to other blood components (Levy et al., 2018). This

elevated risk is an inherent consequence of their required storage conditions, which create a biologically favorable environment for bacterial proliferation. Unlike refrigerated red cells or frozen plasma, RT-stored platelets in gas-permeable bags with continuous agitation support the rapid exponential growth of many bacteria, including common skin flora introduced during venipuncture (Jacobs et al., 2024; Ketter et al., 2019). Even low initial inocula (1–10 colony-forming units) can expand to clinically dangerous levels over the standard 4–7-day shelf life (Cloutier & De Korte, 2022).

Despite the implementation of multilayer safety interventions—including rigorous donor selection, optimized arm disinfection, diversion pouches to sequester the initial skin plug, and sensitive bacterial culture strategies—a residual risk persists. Estimates suggest that approximately 1 in 1,000 to 1 in 2,500 platelet components is contaminated at the time of collection (Levy et al., 2018). Following mitigation, the risk of a septic transfusion reaction (STR) remains the leading infectious threat in modern transfusion medicine. Contemporary hemovigilance data estimate the residual contamination risk at approximately 1 in 10,000 platelet products, the risk of a non-fatal STR at 1 in 100,000, and a fatal STR at 1 in 500,000 (Bloch et al., 2018; García-Otálora et al., 2025). This stands in stark contrast to the modeled residual risks for major viral infections, which are now well below 1 in a million, underscoring the disproportionate concentration of infectious risk within the platelet inventory (Bloch et al., 2018).

The persistence of this risk is attributed to a confluence of factors: sampling error in culture-based detection, the presence of slow-growing or biofilm-forming organisms that evade initial detection, the relative resistance of spore-forming bacteria to some mitigation strategies, and rare post-testing contamination events (Cloutier & De Korte, 2022; O'Flaherty et al., 2023). Consequently, room-temperature-stored platelets are consistently identified as the dominant source of transfusion-associated sepsis in contemporary practice (Levy et al., 2018).

### 2.2 Pathogen Reduction Technologies: Substantial Reduction Without Elimination

Pathogen reduction technologies (PRTs) represent a paradigm shift from reactive, detection-centered screening to a proactive, product-centered safety layer. These technologies utilize ultraviolet



light combined with photosensitizers (e.g., amotosalen, riboflavin) or UVC light alone to damage nucleic acids, thereby inactivating a broad spectrum of pathogens—including bacteria, viruses, and parasites—within the entire blood component (Liu & Wang, 2021; Rezvany et al., 2024). This approach fundamentally complements, rather than replaces, existing donor screening and bacterial testing protocols.

Evaluated by  $\log_{10}$  reduction factors, PRTs demonstrate high efficacy, achieving  $>5-7 \log_{10}$  reduction against most vegetative bacteria (Lu & Fung, 2020). Real-world data from large-scale implementations confirm their significant impact. For instance, the nationwide implementation of 100% amotosalen/UVA PRT in France reduced the TTBI rate from 1 in 92,687 to 1 in 1,645,295 platelet components—a more than tenfold reduction (Richard et al., 2023). Hemovigilance data from major blood services consistently indicate that PRT, when added to standard controls, significantly enhances product safety (García-Otálora et al., 2025).

However, it is critical to recognize that PRT does not eliminate risk entirely. Biological limitations exist, including lower efficacy against bacterial spores, some non-enveloped viruses, and biofilm-associated organisms (Levy et al., 2018). Furthermore, PRT cannot neutralize pre-formed toxins or prevent contamination introduced after the treatment process. Documented cases of breakthrough sepsis, often linked to post-processing bag damage or environmental contamination, delineate a "floor" of residual risk and confirm that PRT is not a sterilization step (Frideric et al., 2020; Prioli et al., 2018). This persistent residual risk, even after substantial intervention, mirrors the structural "workforce fragilities" described by Atento et al. (2025b), who note that systemic constraints in global health create a 'hard floor' of residual risk that cannot be eliminated by a single-point solution. Thus, while PRT substantially lowers the bacterial risk profile, it functions most effectively as part of an integrated safety strategy that includes optimized manufacturing and robust process controls (Cloutier & De Korte, 2022).

### **2.3 Comparative Analysis of PRT Platforms: Mechanisms and Impact on Platelet Quality**

The three leading PRT platforms—Intercept (amotosalen/UVA), Mirasol (riboflavin/UVB-weighted broad-spectrum UV), and Theraflex (UVC-only)—share a nucleic-acid-targeting

mechanism but differ in their photosensitizer, UV spectrum, and workflow, leading to nuanced differences in platelet quality outcomes (Diallo et al., 2020; Levy et al., 2018).

Mechanistically, Intercept induces cross-links in nucleic acids and requires a compound adsorption device (CAD) step for residual chemical removal, a process that lengthens processing time and can lead to greater platelet loss (Malvaux et al., 2022; Rebullá, 2019). Mirasol, in contrast, causes guanine oxidation and single-strand breaks via riboflavin and UV light, offering a simpler workflow with no removal step, as riboflavin and its photoproducts are physiological (Diallo et al., 2020). Theraflex, still in earlier stages of adoption, uses direct UVC damage without additives (Rebullá, 2019).

In vitro comparative studies reveal platform-specific impacts on the progression of the platelet storage lesion. Head-to-head comparisons indicate that Mirasol-treated platelets often exhibit a more pronounced metabolic lesion by Day 7, characterized by higher lactate generation, faster glucose depletion, elevated phosphatidylserine exposure (Annexin V), and earlier loss of swirling compared to Intercept-treated units (Malvaux et al., 2022; Rozhkov et al., 2023). While ultrastructural studies show no major additional mitochondrial damage from either technology beyond standard storage effects, subtler differences exist, such as altered microRNA profiles in platelet-derived microparticles from Intercept-treated units (Barham et al., 2025; Diallo et al., 2020).

Clinically, meta-analyses of randomized controlled trials suggest that Intercept-treated platelets maintain hemostatic efficacy comparable to conventional platelets, despite lower post-transfusion increments (Cid et al., 2024; Garban et al., 2018). In contrast, Mirasol-treated platelets have been associated with a modest but significant increase in WHO grade  $\geq 2$  bleeding in some trials, correlating with the observed in vitro quality decrement (Cid et al., 2024; Van Der Meer et al., 2018). Therefore, the choice of platform involves balancing logistical simplicity, regulatory maturity, and tolerance for subtle but meaningful differences in platelet quality and clinical performance.

### **2.4 Mirasol PRT and Platelet Viability Through Day 7**

While Mirasol-treated platelets can often meet formal regulatory quality control (QC) thresholds for extended storage to Day 7, a consensus from



multiple studies indicates borderline or degraded functional quality by that time (Escolar et al., 2021; Valsami et al., 2022). Key viability markers such as pH may remain above the critical lower limit of 6.2–6.4, but other indicators show significant, clinically relevant decline.

Studies tracking platelets through storage note that swirling—a simple macroscopic marker of platelet discoid morphology and viability—is frequently reduced or lost in Mirasol-treated units by Day 5–7 (Malvaux et al., 2022; Valsami et al., 2022). Concurrently, markers of platelet activation (e.g., P-selectin/CD62P) and apoptosis (Annexin V binding) increase more markedly compared to untreated or Intercept-treated platelets (Escolar et al., 2021; Lachert et al., 2018). Molecular analyses support this accelerated lesion, with proteomic and extracellular vesicle (EV) profiling of Day-7 Mirasol platelets revealing signatures of hyperactivation, oxidative stress, and deregulated metabolism (Hermida-Nogueira et al., 2020; Salunkhe et al., 2019).

The operational interpretation of these findings is critical: satisfying basic numeric QC parameters does not equate to preserved *in vivo* function. The loss of swirling, increased activation, and apoptosis suggest reduced post-transfusion recovery and survival (Liu et al., 2023). This gap between a 'technically compliant' product and its 'biologically degraded' state echoes the 'narrative-analytic gap' described by Atento et al. (2025c), who argue that quantitative healthcare data must be mediated by qualitative, patient-centered narratives to fully capture clinical reality and avoid interpretive flattening. Consequently, many blood services, supported by comparative *in vitro* data, restrict the routine shelf life of riboflavin/UV-treated platelets to 5 days, reserving Day-7 storage for inventory management purposes rather than assuming equivalent clinical efficacy (Malvaux et al., 2022).

### **2.5 Impact of Mirasol PRT on Plasma Coagulation Integrity**

When applied to plasma, Mirasol PRT induces a measurable but generally clinically acceptable reduction in coagulation factor activity. A focused review indicates typical decreases of approximately 21–23% in fibrinogen and 25–31% in factor VIII (FVIII), with more modest reductions in other factors (Wasiluk et al., 2020). These changes manifest as mild to moderate prolongations of prothrombin time (PT) and activated partial

thromboplastin time (aPTT) (Rosell-Valle et al., 2022; Sherstyukova et al., 2025).

Despite these reductions, the hemostatic integrity of the plasma is largely preserved. Global coagulation assays, such as thromboelastometry, often remain within reference ranges post-treatment, indicating maintained overall clotting capacity (Sherstyukova et al., 2025). This is because the post-PRT factor levels, while reduced, typically remain within the wide normal physiological range (50–150% of standard) and are sufficient to correct coagulopathies at standard therapeutic dosing (Mokhtarian et al., 2025). Natural anticoagulants like protein C and antithrombin are generally well preserved (Wasiluk et al., 2020).

The operational implication is that Mirasol-treated plasma retains clinical utility for most indications. However, in high-acuity scenarios requiring maximal factor delivery per unit—such as severe coagulopathy with volume restriction—the 20–30% reduction in key factors may necessitate marginally higher plasma dosing to achieve therapeutic targets. This integrated perspective, where safety gains are weighed against quality costs, aligns with the 'dual outcomes' framework proposed by Atento et al. (2025a), who argue that healthcare organizations must simultaneously optimize clinical and business outcomes through integrated analytics. This trade-off between pathogen safety and hemostatic potency is well-recognized, with next-generation technologies like visible-light PRT showing promise for further minimizing factor loss (Stewart et al., 2024).

### **2.6 Operational Impact of PRT on Shelf Life, Wastage, and Inventory Resilience**

The operational impact of implementing PRT on platelet wastage and supply resilience is profoundly influenced by whether the technology is coupled with an extension of shelf life. Evidence clearly demonstrates that PRT with shelf-life extension (e.g., from 5 to 7 days) leads to significant reductions in outdated and improved inventory buffering. Real-world implementations in Spain and Brazil reported outdate rate reductions of 88–100% and from 6% to 1.2%, respectively, following the move to 7-day PRT platelets (Fachini et al., 2021; Gorria et al., 2019; Jimenez-Marco et al., 2018). Simulation models at national levels corroborate that longer shelf life decreases expiry rates and unmet demand while lowering required inventory levels (Dillon et al., 2023; Ramirez-Arcos et al., 2020).



Conversely, PRT implementation without shelf-life extension, or with an effective shortening of usable life, can negatively impact logistics. A Canadian simulation modeling 5-day PRT pooled platelets (with an effective usable life of 3–4 days) alongside 7-day conventional apheresis platelets predicted increased wastage and shortages, necessitating a rise in collections to maintain service levels (Blake et al., 2021; Rebullà & Prati, 2022).

Therefore, the key determinant of PRT's operational benefit is not the technology alone, but its integration within a system that includes inventory optimization, donor scheduling, and often, an authorized shelf-life extension. When these conditions are met, PRT can transform platelet inventory management by reducing waste, improving cost-effectiveness, and strengthening resilience against demand fluctuations and supply shocks (Aliaga et al., 2024; Zhang et al., 2022). The conditionality of these operational benefits—where PRT alone is insufficient without aligned inventory and policy frameworks—is conceptually similar to the strategic challenges faced by dominant incumbents like Mercury Drug, whose ability to leverage digital transformation is conditional on developing dynamic capabilities alongside legacy strengths (Atento & Atento, 2025).

## 2.7 Synthesis of Literature and Literature Gaps

### *Synthesis of the Literature*

The literature converges on a stable point of departure: room-temperature platelet concentrates remain the most consequential residual infectious vulnerability in contemporary transfusion practice, and this is not merely a procedural deficiency but a structural feature of platelet logistics. Because platelets must be stored at 20–24°C under agitation in gas-permeable bags, they occupy a biologically permissive niche for bacterial amplification that refrigerated red cells and frozen plasma largely avoid (Levy et al., 2018; Jacobs et al., 2024; Ketter et al., 2019). This storage ecology makes even very low inocula operationally meaningful; the repeated observation that 1–10 CFU can expand to dangerous loads within a typical 4–7-day window explains why residual risk persists even under multilayer controls (Cloutier & De Korte, 2022). Importantly, hemovigilance-based risk estimates—contamination at collection on the order of 1 in 1000–2500 and clinically significant septic transfusion reactions remaining the leading infectious threat—anchor the platelet problem as a dominant safety issue despite the near-elimination of

major viral risks to below 1 in a million (Levy et al., 2018; Bloch et al., 2018; García-Otálora et al., 2025).

Within this context, pathogen reduction technologies (PRTs) are consistently framed as a product-centered, proactive risk-control layer that complements (rather than replaces) donor screening and bacterial testing (Liu & Wang, 2021; Rezvany et al., 2024). Their core contribution is conceptual as well as practical: they shift the safety strategy from "detecting contaminated units" toward "reducing the probability that viable pathogens remain capable of replication." Efficacy evidence, typically expressed as  $\log_{10}$  reduction factors and supported by real-world hemovigilance after large-scale implementation, suggests that PRT can reduce TTBI rates by an order of magnitude or more in practice (Lu & Fung, 2020; Richard et al., 2023; García-Otálora et al., 2025). However, the literature is equally explicit that PRT is not sterilization. Biological constraints (e.g., spores, some biofilm-associated organisms, some non-enveloped viruses) and process realities (e.g., inability to neutralize preformed toxins; contamination introduced after treatment; bag damage) define a hard "floor" of residual risk (Levy et al., 2018; Prioli et al., 2018; Fridey et al., 2020; Cloutier & De Korte, 2022). The contemporary consensus is therefore "substantial reduction without elimination," which has direct implications for how study findings should be interpreted and claimed.

A second synthesis emerges when the literature moves from safety efficacy to component quality, particularly for platelet concentrates. Comparative analyses show that Intercept, Mirasol, and Theraflex share nucleic-acid targeting but differ in photosensitizer requirements, UV wavelength profiles, and workflow steps; these differences shape platelet yield and the trajectory of the storage lesion (Diallo et al., 2020; Levy et al., 2018; Rebullà, 2019). Intercept's CAD step increases process complexity and can reduce yield, but comparative evidence suggests that some in vitro quality parameters may remain better preserved among the treated product than is sometimes observed with Mirasol (Malvaux et al., 2022; Rozhkov et al., 2023). For Mirasol, the literature repeatedly describes a tendency toward earlier or more pronounced metabolic and activation signatures by Day 7—higher lactate, faster glucose depletion, increased Annexin V binding, and earlier loss of swirling—consistent with an "accelerated storage lesion" profile in some head-to-head comparisons



(Malvaux et al., 2022; Rozhkov et al., 2023). Clinically, the literature suggests that Intercept-treated platelets generally preserve hemostatic efficacy despite lower increments, whereas some trials of Mirasol-treated platelets have reported modest increases in moderate bleeding categories (Cid et al., 2024; Garban et al., 2018; Van Der Meer et al., 2018). The unifying analytic implication is that pathogen reduction decisions are best modeled as a safety–quality trade-off, with platform choice affecting the trade-off's slope rather than eliminating it.

The Mirasol-specific literature refines this trade-off by clarifying what "viability" should mean. Although Day-7 storage is often feasible in the sense that pH thresholds can remain above minimum QC cutoffs, the literature indicates that numeric acceptability does not guarantee preserved *in vivo* function (Escolar et al., 2021; Valsami et al., 2022). Swirling loss, increasing activation (CD62P), apoptosis signals (Annexin V), and molecular signatures of oxidative stress and dysregulated metabolism converge on the idea that Day-7 Mirasol platelets may be "technically compliant" yet biologically degraded in clinically relevant ways (Malvaux et al., 2022; Hermida-Nogueira et al., 2020; Salunkhe et al., 2019; Liu et al., 2023). This helps explain why some blood services restrict routine shelf life to 5 days, reserving Day-7 inventory primarily for logistics rather than assuming equivalence in clinical performance (Malvaux et al., 2022).

For plasma, the synthesis is comparatively more permissive but still trade-off oriented. Mirasol-treated plasma demonstrates measurable factor attenuation—often reflected in mild-to-moderate PT/aPTT prolongation and reductions in fibrinogen and FVIII—while global assays and the broad physiological range of coagulation factors support the interpretation that many clinical indications remain adequately served under standard dosing (Wasiluk et al., 2020; Rosell-Valle et al., 2022; Sherstyukova et al., 2025; Mokhtarian et al., 2025). Yet the literature also anticipates context-dependent sensitivity: in severe coagulopathy with volume restriction, a 20–30% loss in key factors may matter operationally (Sherstyukova et al., 2025). Emerging visible-light approaches are positioned as a potential pathway to reduce this potency loss, reinforcing the field's implicit goal: preserve safety gains while flattening the quality penalty (Stewart et al., 2024).

Finally, the literature makes clear that operational claims about wastage reduction are conditional. When PRT is coupled with an authorized shelf-life extension, outdate reductions can be dramatic and inventory resilience improves; when extension is absent or "effective usable life" is shortened by quality decline, models predict increased shortages and wastage (Fachini et al., 2021; Gorria et al., 2019; Jimenez-Marco et al., 2018; Dillon et al., 2023; Ramirez-Arcos et al., 2020; Blake et al., 2021; Rebullà & Prati, 2022). Therefore, the operational argument is not simply "PRT reduces wastage," but rather: PRT can reduce wastage if biological viability and regulatory policy enable longer usable life and if inventory optimization is aligned with that usable life.

#### *Literature Gaps*

Gap 1: Persistent residual risk is well described, but "residual risk after PRT" is under-theorized at the operational level. The literature acknowledges breakthrough events and non-elimination scenarios (e.g., spores, post-treatment contamination, bag damage), but there remains limited analytic treatment of what occasional failure implies for routine implementation: whether it reflects biological resistance, process deviation, sampling limitations, or post-processing contamination pathways (Levy et al., 2018; Prioli et al., 2018; Fridey et al., 2020). This gap is consequential because it determines whether a rare positive culture in a controlled context should be interpreted as a technology limitation, a procedural control issue, or a monitoring artifact.

Gap 2: Viability is frequently discussed as a broad construct, yet many applied evaluations rely on a narrow subset of indicators. The literature emphasizes multiparametric viability (pH, swirling, activation/apoptosis markers, aggregation/HSR), but the evidence base also includes pragmatic studies that are necessarily constrained to routine blood bank measures (Valsami et al., 2022; Salunkhe et al., 2019; Liu et al., 2023). There is therefore a gap in disciplined interpretation: how to draw appropriately bounded conclusions when viability is operationalized through storage indicators rather than direct functional endpoints.

Gap 3: Platform comparisons exist, but context-specific replication remains necessary. Comparative work indicates that Mirasol may show a more pronounced storage lesion profile by Day 7



in some settings, while Intercept may preserve selected indicators despite additional processing steps (Malvaux et al., 2022; Rozhkov et al., 2023). However, platelet preparation protocols, additive solutions, storage logistics, and bacterial monitoring systems vary across services, meaning local evaluations remain relevant to confirm how the trade-off manifests within a specific workflow environment.

Gap 4: Plasma "clinical acceptability" is often asserted in aggregate, while parameter-specific persistence and magnitude require clearer framing. The literature generally supports clinical utility despite measurable factor reductions, yet decision-relevant interpretation depends on the magnitude of fibrinogen/FVIII loss, persistence after storage, and the clinical contexts most sensitive to potency dilution (Wasiluk et al., 2020; Sherstyukova et al., 2025; Mokhtarian et al., 2025). Evaluations that quantify pre/post and post-storage changes help ground this trade-off more precisely.

Gap 5: Inventory models highlight shelf-life sensitivity, but empirical quality trajectories are not always integrated into operational claims. Operational studies show large improvements when 7-day storage is feasible and used, but the biological literature warns that "meeting QC thresholds" may not imply equivalently functional platelets at Day 7 (Dillon et al., 2023; Blake et al., 2021; Malvaux et al., 2022; Valsami et al., 2022). The gap is integrative: aligning biological usable life (as indicated by storage lesion trajectories) with inventory usable life (as assumed in logistics models) to avoid overpromising system-level benefits.

Gap 6 (New): The literature lacks an integrated framework for conceptualizing the parallel trade-offs in blood safety and broader healthcare systems. While the technical aspects of PRT are well-documented, there is a need for analytic models that connect these micro-level component changes to macro-level system outcomes, a gap that cross-disciplinary frameworks from health analytics and strategic management could help address (Atento et al., 2025a; Atento & Atento, 2025).

#### *Bridging Statement to the Present Study*

Taken together, the literature supports pathogen reduction as a major advance in mitigating platelet-associated bacterial risk while

simultaneously establishing that residual risk and component-quality trade-offs remain unavoidable and platform-dependent. These tensions motivate an in vitro evaluation of Mirasol-treated platelets and plasma that jointly examines (a) bacterial suppression under controlled challenge conditions, (b) changes in platelet storage indicators across storage time points, and (c) parameter-specific shifts in plasma coagulation tests before treatment, after treatment, and after frozen storage. By anchoring interpretations to clearly defined endpoints and explicitly treating findings as evidence of a safety-quality balance rather than a categorical solution, the study contributes context-specific evidence relevant to both transfusion safety strategy and operational decision-making.

### **3. Materials and Methods**

#### **3.1 Study design**

An in vitro experimental design with pre-post and repeated-measures assessments was employed to evaluate the effects of Mirasol Pathogen Reduction Technology (Mirasol PRT) on (a) bacterial suppression and selected storage indicators in platelet concentrates and (b) coagulation screening parameters in plasma. Platelet outcomes were monitored across defined storage time points, and plasma outcomes were measured before treatment, after treatment, and after frozen storage.

#### **3.2 Study setting**

All component preparation and laboratory procedures were performed within a controlled blood component processing and laboratory environment, including aseptic transfers performed using sterile connection techniques.

#### **3.3 Materials and instruments**

Key materials and equipment included: the Mirasol PRT system and riboflavin solution (500  $\mu\text{mol/L}$ ); a sterile connecting device and closed-system transfer bags; a Helmer platelet incubator/agitator for platelet storage; a Helmer freezer ( $\leq -18^\circ\text{C}$ ) for plasma storage; a pH meter (HI8417) for platelet pH measurement; an automated hematology analyzer (Cell Dyn Emerald) for platelet count determination; and an automated blood culture detection system using aerobic BACTEC Plus bottles monitored by the Bactec FX



platform. Coagulation parameters were determined using the Sysmex CS-2000i/CS-2100i system.

### 3.4 Samples and preparation

#### *Platelet concentrates*

Ten pooled platelet concentrate samples were prepared. Each pooled unit was created by combining five interim platelet units suspended in platelet additive solution (T-PAS) using a closed system with sterile connecting technique. The resulting pooled platelet concentrate volume was approximately  $250 \pm 30$  mL.

#### *Plasma units*

Ten single-unit plasma samples were prepared from whole blood donations collected using the Reveos LR set and processed on the Reveos 3C system. Whole blood units were held overnight prior to centrifugation and separation into components. Final plasma unit volume was approximately  $280 \pm 30$  mL.

### 3.5 Bacterial strain and inoculum preparation

The bacterial challenge organism used for platelet inoculation was *Staphylococcus aureus* ATCC 25923. A working suspension was prepared to yield a target concentration of 30 CFU/mL for inoculation.

### 3.6 Platelet inoculation, controls, and pathogen reduction procedure

For each pooled platelet concentrate:

- a. Negative control (uninoculated) aliquot: Prior to inoculation, a 20 mL aliquot was aseptically removed from the platelet pool into a transfer bag to serve as a negative control.
- b. Inoculation: The pooled platelet concentrate was inoculated with 0.5 mL of the 30 CFU/mL working suspension using aseptic technique.
- c. Positive control (inoculated, untreated) aliquot: After inoculation, a 30 mL aliquot was aseptically removed into a transfer bag to serve as a positive (untreated) control.
- d. Pre-treatment hold: The remaining inoculated platelet unit was held for 2

hours after inoculation prior to pathogen reduction treatment.

- e. Riboflavin addition: 35 mL of riboflavin solution ( $500 \mu\text{mol/L}$ ) was aseptically added to the inoculated platelet unit using sterile connection technique.
- f. Mirasol PRT illumination: Following riboflavin addition, the platelet unit was treated in the Mirasol system in accordance with the manufacturer's instructions for use for platelet concentrates.

### 3.7 Platelet storage conditions and time points

Treated platelet units were stored in a platelet incubator/agitator at  $20\text{--}24^\circ\text{C}$  under standard conditions and monitored through Day 7. Platelet pH and platelet count were measured before treatment (baseline) and after treatment on Day 0, Day 3, and Day 7.

### 3.8 Bacterial detection and culture monitoring

Bacterial detection was performed using an automated culture system. Aseptically collected samples (10 mL) were inoculated into aerobic BACTEC Plus culture bottles and monitored using the Bactec FX system. The monitoring period for inoculated bottles was 7 days. Testing was conducted to evaluate bacterial persistence in the inoculated untreated controls and the treated platelet units at the specified time points described in the protocol.

### 3.9 Plasma pathogen reduction, storage, and testing schedule

- a) Baseline sampling. A 10 mL aliquot was collected before Mirasol treatment for baseline coagulation testing.
- b) Riboflavin addition. 35 mL riboflavin solution ( $500 \mu\text{mol/L}$ ) was aseptically added.
- c) Illumination. The unit was treated using Mirasol PRT in accordance with the manufacturer's instructions for use for plasma.
- d) Post-treatment sampling. A second 10 mL aliquot was collected after treatment for post-treatment coagulation testing.



- e) Frozen storage. Remaining treated plasma was stored frozen at  $\leq -18^{\circ}\text{C}$ .
- f) Post-storage testing. After 30 days, plasma was thawed and re-tested.

### 3.10 Outcome measures

#### *Platelet storage indicators (viability proxies)*

Platelet viability was operationalized using:

- a. pH (pH meter HI8417), and
- b. platelet count (Cell Dyn Emerald hematology analyzer),

measured at baseline and at Day 0, Day 3, and Day 7 after treatment.

#### *Plasma coagulation parameters (integrity proxies)*

Plasma integrity was operationalized using:

- a. Prothrombin time (PT),
- b. Activated partial thromboplastin time (aPTT), and
- c. Fibrinogen activity,

measured before treatment, after treatment, and after 30 days of frozen storage using the Sysmex CS-2000i/CS-2100i system.

### 3.11 Statistical analysis

All study data were encoded and analyzed using SPSS version 26. Repeated-measures analysis of variance (repeated-measures ANOVA) was applied to evaluate within-unit changes over time in platelet storage indicators (pH, platelet count) and plasma coagulation parameters (PT, aPTT, fibrinogen) across the defined measurement points (before treatment and subsequent time points post-treatment and/or post-storage, depending on the analyte). Descriptive statistics (mean and standard deviation) were generated for each time point as the basis for interpretation and for profiling temporal patterns. Statistical significance was evaluated at  $\alpha = 0.05$ .

Assumptions for repeated-measures modeling were examined using Mauchly's test of sphericity. Where sphericity was not satisfied, corrected degrees of freedom were applied using the Greenhouse-Geisser and/or Huynh-Feldt epsilon adjustments, consistent with the SPSS repeated-

measures output set. Effect magnitude was summarized using partial eta squared as provided in the model outputs. When omnibus time effects were statistically significant, estimated marginal means and pairwise comparisons generated by SPSS were used to localize differences across time points, consistent with the model's repeated-measures structure.

### 3.12 Ethical Considerations

Ethical approval for the study protocol was obtained from the Medical Research Center-HMC, Doha, Qatar (case number 1187).

All component handling and sampling were performed using closed-system techniques with sterile connection procedures to minimize contamination and maintain biosafety. Procedures involving bacterial propagation and inoculation were conducted under controlled conditions, including use of a biosafety cabinet and disinfection of sampling sites prior to inoculation and sampling to reduce procedural contamination risk

## 4. Results and Discussion

### 4.1 pH of platelet concentrates after MPRT treatment and during storage

Across the 10 pooled platelet concentrates, pH declined progressively from pre-treatment baseline through the storage period following Mirasol Pathogen Reduction Technology (MPRT). At baseline, pH values ranged from 7.14 to 7.28 with a mean of 7.204. Immediately after treatment (Day 0), values shifted downward to a range of 7.07 to 7.22 (mean 7.142). By Day 3, pH exhibited a pronounced reduction, clustering tightly between 6.77 and 6.94 (mean 6.839). By Day 7, the mean remained similarly low (6.829), with a wider observed range (6.62 to 7.22), indicating greater dispersion late in storage relative to earlier time points.

A repeated-measures ANOVA indicated that mean pH differed significantly across time points ( $F = 64.239$ ,  $p < .001$ ), with a large within-subject effect (partial  $\eta^2 = .877$ ), consistent with a strong time-associated shift in pH during storage following treatment.

Post-hoc comparisons showed that the pH reductions were statistically significant for comparisons involving baseline, Day 0, and Day 3/Day 7 (all  $p < .001$ ). In contrast, the comparison between Day 3 and Day 7 was not statistically

significant ( $p = 1.000$ ), suggesting that the largest decrement occurred by Day 3, after which the group mean stabilized through Day 7 despite increased variability in individual values at the final time point.

#### **4.2 Platelet count of concentrates after MPRT treatment and during storage**

Platelet count demonstrated a clear downward trajectory across storage time points. At baseline, platelet counts ranged from 924 to  $1565 \times 10^3/\mu\text{L}$  (mean  $1296.6 \times 10^3/\mu\text{L}$ ). At Day 0, values ranged from 868 to  $1397 \times 10^3/\mu\text{L}$  (mean  $1199.0 \times 10^3/\mu\text{L}$ ). By Day 3, the range was 828 to  $1388 \times 10^3/\mu\text{L}$  (mean  $1120.8 \times 10^3/\mu\text{L}$ ). By Day 7, the platelet count range contracted to 683 to  $1079 \times 10^3/\mu\text{L}$  (mean  $879.4 \times 10^3/\mu\text{L}$ ). Collectively, this reflects a net mean reduction of approximately  $417 \times 10^3/\mu\text{L}$  from baseline to Day 7 (roughly one-third of the baseline mean).

A repeated-measures ANOVA indicated statistically significant differences in platelet counts over time ( $F = 43.958$ ,  $p < .001$ ), with a substantial within-subject effect (partial  $\eta^2 = .830$ ), indicating that time accounted for a large proportion of within-unit variation in platelet count across the repeated measurements.

Pairwise comparisons indicated that baseline differed significantly from Day 0 ( $p = .008$ ), Day 3 ( $p = .002$ ), and Day 7 ( $p < .001$ ). In addition, Day 0 differed from Day 3 ( $p = .046$ ) and Day 7 ( $p < .001$ ), and Day 3 differed from Day 7 ( $p = .003$ ). This pattern indicates that platelet count decline was already evident immediately after treatment (baseline to Day 0), continued modestly through Day 3, and then showed the most substantial separation by Day 7, when counts were consistently lower across all pools than earlier time points.

#### **4.3 Bacterial detection following inoculation and MPRT treatment**

Bacterial culture findings showed that, following inoculation of pooled platelet concentrates with 15 CFU of *Staphylococcus aureus* (ATCC 25923) and subsequent MPRT treatment, 9 of 10 treated platelet pools remained culture-negative after 7 days of incubation in the automated blood culture system. One treated pool (platelet pool 4) yielded a culture-positive result at Day 7, indicating incomplete elimination of bacterial contamination in that specific pool under the described conditions; this corresponds to an

observed elimination effectiveness of 90% across the treated pools in this dataset.

Control results supported the interpretability of the culture findings. A positive control pool that did not undergo MPRT was culture-positive within 24 hours, and remained positive at Day 7, consistent with bacterial viability and detectability under the incubation conditions. A separate positive control (inoculated then incubated for 7 days without treatment) was likewise culture-positive at Day 7. Meanwhile, negative controls were culture-negative after 7 days of incubation, supporting the absence of background contamination in the testing workflow.

#### **4.4 Coagulation factor measurements in plasma following MPRT and freezing**

Across the 10 plasma units, coagulation parameters shifted measurably after MPRT and following freezing through Day 30. Prothrombin time (PT) increased from a baseline mean of 10.91 s (range 10.0–11.7) to 12.63 s at Day 0 (range 11.3–14.3), and to 13.15 s at Day 30 (range 11.7–15.5). Activated partial thromboplastin time (aPTT) similarly increased from a baseline mean of 29.03 s (range 26.7–31.8) to 33.46 s at Day 0 (range 30.7–37.9) and 34.37 s at Day 30 (range 31.5–38.8). In contrast, fibrinogen decreased markedly from a baseline mean of 2.756 g/L (range 1.80–4.44) to 1.445 g/L at Day 0 (range 0.92–2.31) and 1.555 g/L at Day 30 (range 1.05–2.32).

Repeated-measures ANOVA indicated statistically significant differences over time for PT ( $F = 84.377$ ,  $p < .001$ ), aPTT ( $F = 112.96$ ,  $p < .001$ ), and fibrinogen ( $F = 84.846$ ,  $p < .001$ ), establishing that the observed shifts across baseline, Day 0, and Day 30 were unlikely to be attributable to random within-unit fluctuation alone.

Pairwise comparisons clarified the structure of these time-associated changes. For PT, the mean increase from baseline to Day 0 was +1.720 s ( $p < .001$ ), and from baseline to Day 30 was +2.240 s ( $p < .001$ ); the additional difference between Day 0 and Day 30 was smaller (+0.520 s,  $p = .001$ ).

For aPTT, increases were similarly structured: baseline to Day 0 was +4.430 s ( $p < .001$ ), baseline to Day 30 was +5.340 s ( $p < .001$ ), and Day 0 to Day 30 was +0.910 s ( $p < .001$ ), indicating that most of the shift occurred immediately after treatment with a smaller—but still statistically detectable—increment through Day 30.



For fibrinogen, the dominant change was the large post-treatment decrease: baseline to Day 0 showed a mean reduction of 1.311 g/L ( $p < .001$ ), and baseline to Day 30 showed a reduction of 1.201 g/L ( $p < .001$ ). The Day 0 versus Day 30 comparison indicated a smaller mean difference of 0.110 g/L ( $p = .001$ ), reflecting a relatively modest separation between immediate post-treatment and Day 30 values compared with the magnitude of the baseline-to-post-treatment decline.

Taken together, these pairwise results indicate that the primary inflection for all three coagulation parameters occurred between baseline and Day 0 (i.e., immediately after treatment), whereas the baseline-to-Day 30 profile largely reflected persistence of those post-treatment shifts with comparatively smaller additional divergence over the frozen storage interval.

#### 4.5 Summary of patterns across endpoints

Taken together, the platelet and plasma findings demonstrate a consistent “two-layer” pattern: (a) an immediate post-treatment shift detectable at Day 0, followed by (b) time-dependent storage effects whose magnitude and shape depend on the endpoint.

For platelet storage indicators, the most salient feature was that deterioration was not linear across time. Platelet pH showed a marked decline from baseline through Day 3 and then stabilized at the group level through Day 7, as reflected by the non-significant Day 3 versus Day 7 contrast ( $p = 1.000$ ) despite significant differences across the full set of time points (overall  $p < .001$ ). In contrast, platelet count declined progressively across the entire storage horizon, including a pronounced separation by Day 7 (overall  $p < .001$ ; multiple pairwise contrasts significant). This divergence between pH “plateauing” and platelet count continuing to fall suggests that the study’s two viability proxies were capturing different aspects of storage-associated change: pH reflected an early metabolic shift that reached a lower steady-state, while platelet count reflected cumulative attrition over time.

For bacterial suppression, the control results established internal validity of the challenge-and-detection workflow: negative controls remained negative, whereas untreated inoculated controls became positive early and remained positive. Against this control backdrop, the treated platelet outcomes indicated that most treated pools did not yield detectable growth at Day 7, while a single

treated pool became culture-positive at Day 7, corresponding to a 9/10 culture-negative proportion under the study’s conditions. Importantly, this positivity pattern was not diffuse (i.e., not multiple intermittent positives), but rather concentrated in one treated pool with late detection—an outcome structure that is analytically distinct because it points to generally effective suppression in most units alongside occasional late breakthrough detectable under prolonged incubation.

For plasma coagulation parameters, the dominant inflection occurred immediately after treatment (baseline to Day 0), with smaller additional shifts after frozen storage (Day 0 to Day 30), although these latter increments were still statistically detectable. PT and aPTT showed the same directional profile—prolongation after treatment with further modest prolongation after storage—whereas fibrinogen exhibited a large post-treatment reduction with relative stability thereafter (only a small Day 0 to Day 30 difference compared with the baseline-to-post-treatment change). In magnitude terms, the mean fibrinogen reduction was substantial (approximately halving from baseline), while clotting times increased by several seconds, indicating that the PRT process produced a coherent coagulation shift observable across multiple screening markers rather than an isolated change in a single parameter.

Overall, the results collectively characterize Mirasol PRT as producing (1) strong bacterial suppression in most treated platelet pools, (2) measurable storage-associated changes in platelet indicators that intensify with time, and (3) an immediate, sustained alteration of plasma coagulation screening results that persists through a 30-day frozen storage interval, with additional but smaller drift after storage.

#### 4.6 Discussion of Findings

##### 4.6.1 Interpreting bacterial suppression within the reality of residual platelet risk

The bacterial results should be interpreted against the established transfusion-safety context in which room-temperature platelets remain the dominant residual infectious risk in modern transfusion medicine (Levy et al., 2018; Jacobs et al., 2024). This risk is structurally driven by platelet storage biology: platelets are stored at 20–24°C under agitation in gas-permeable bags, which enables bacterial amplification during the usable storage period (Ketter et al., 2019; Cloutier & De



Korte, 2022). Even under contemporary layered controls, hemovigilance consistently positions septic transfusion reaction as the leading residual infectious threat relative to viral risks, which are now modeled well below one in a million (Bloch et al., 2018; García-Otálora et al., 2025).

Within this context, the observation that 9 of 10 Mirasol-treated platelet pools were culture-negative at Day 7 indicates substantial bacterial suppression under the study's controlled challenge and monitoring conditions. This aligns with the literature that frames pathogen reduction technologies as a proactive product-centered safety layer with high log-reduction performance against most vegetative bacteria (Lu & Fung, 2020; Liu & Wang, 2021; Rezvany et al., 2024). Moreover, the control findings (negative controls remaining negative; inoculated untreated controls turning positive early and remaining positive) strengthen interpretability by demonstrating that the inoculation and detection workflow was able to distinguish viable bacterial growth from procedural contamination or false positivity.

At the same time, the single late-positive culture among treated units is analytically important because it prevents an overstatement of "elimination." This pattern is consistent with the literature's central caution that PRT substantially reduces risk without fully eliminating it, due to biological limitations (e.g., spores, biofilm-associated protection) and process realities (e.g., contamination after treatment, inability to neutralize pre-formed toxins) (Levy et al., 2018; Prioli et al., 2018; Fridey et al., 2020). In other words, the present finding supports the argument that PRT lowers the risk "ceiling," but a non-zero residual floor remains possible under certain conditions—an interpretation aligned with current hemovigilance experience and with the conceptual positioning of PRT as an integrated risk-control layer rather than a sterilization step (Cloutier & De Korte, 2022; García-Otálora et al., 2025).

Importantly, the positivity occurred as a late event (Day 7) rather than as early widespread failure. This late emergence is consistent with mechanisms described in the literature such as low-level survival with delayed outgrowth, organism- or microenvironment-specific effects, or post-processing contamination pathways (O'Flaherty et al., 2023; Cloutier & De Korte, 2022). The practical implication is not that PRT is ineffective, but rather that pathogen reduction should be interpreted as risk

minimization, and that quality systems still matter (e.g., bag integrity, aseptic sampling, storage controls), because PRT cannot compensate for every pathway of late bacterial emergence.

#### *4.6.2 Platelet pH trajectory: early metabolic shift followed by stabilization*

The platelet pH pattern demonstrated a pronounced decline from baseline to Day 3, followed by no statistically significant change between Day 3 and Day 7, even as the overall time effect was significant ( $p < .001$ ). This shape is clinically and operationally meaningful because it suggests that the largest metabolic shift—at least as captured by pH—occurred early during post-treatment storage, with subsequent stabilization at a lower mean level.

In the platelet storage lesion literature, pH is treated as a core viability-related indicator because it reflects metabolic activity and storage environment adequacy, and because very low pH is associated with poor platelet quality (Valsami et al., 2022; Salunkhe et al., 2019). However, the literature also emphasizes that pH is a necessary but insufficient indicator of "viability." Mirasol-treated platelets may remain above minimum pH thresholds through Day 7 while other indicators (swirling, activation, apoptosis markers) show meaningful deterioration earlier (Escolar et al., 2021; Malvaux et al., 2022). In this study, the pH stabilization after Day 3 can be interpreted as a plateauing of net acidification dynamics at the group level, but it cannot be taken as evidence that platelet functional viability is preserved through Day 7. This disciplined interpretation directly addresses an identified literature gap: viability metrics are often discussed broadly, yet many applied studies necessarily use a narrower indicator set, requiring careful boundaries on inference (Valsami et al., 2022; Liu et al., 2023).

#### *4.6.3 Platelet count decline: progressive attrition across the full storage horizon*

In contrast to pH, platelet count demonstrated a progressive decline from baseline through Day 7, with significant pairwise differences across major timepoint contrasts and a substantial overall time effect ( $p < .001$ ). This pattern suggests cumulative attrition in measured platelet concentration across storage, rather than a purely immediate post-treatment shift.



The divergence between pH plateauing (Day 3 vs Day 7 non-significant) and platelet count continuing to decline implies that these two proxies are capturing different facets of storage-associated change. Within the broader platelet storage lesion literature, Mirasol-treated units have been associated with more pronounced metabolic stress and activation profiles by Day 7 compared to some other platforms (Malvaux et al., 2022; Rozhkov et al., 2023). Although platelet count is not a direct functional measure, the observed trajectory is consistent with an intensifying storage lesion over time in which quantitative decline continues even when the pH curve stabilizes. It is also compatible with the operational rationale reported in the literature: some blood services restrict riboflavin/UV-treated platelets to 5 days in routine use, treating Day 7 as an inventory-management extension rather than as a presumption of equivalent product performance (Malvaux et al., 2022).

Crucially, because the study did not measure swirling, activation markers (CD62P), apoptosis markers (Annexin V), or functional assays (aggregation, hypotonic shock response), the discussion must avoid overextending claims about clinical efficacy. Instead, the results should be positioned as evidence that the study's chosen storage indicators reflect measurable time-dependent degradation, consistent with the directionality of the broader literature on Mirasol-related storage lesion acceleration by late storage (Hermida-Nogueira et al., 2020; Salunkhe et al., 2019; Escolar et al., 2021).

#### *4.6.4 Integrating suppression with storage lesion: the safety-quality trade-off becomes explicit*

A central professional contribution of the study is that it demonstrates, within a single design, both sides of the pathogen reduction decision: bacterial suppression is substantial (9/10 culture-negative) while platelet storage indicators deteriorate with time, particularly by Day 7. This duality is the appropriate analytic framing of Mirasol PRT in the current evidence landscape: not as an unqualified improvement, but as a safety gain purchased with measurable quality costs, with platform-specific nuances relative to other PRT systems (Diallo et al., 2020; Rebutta, 2019; Malvaux et al., 2022).

This framing directly connects to the literature gap on how to interpret “residual risk after PRT” operationally. The single late-positive treated pool shows that suppression is strong but not absolute,

which is consistent with the literature's assertion that PRT reduces risk substantially but cannot remove all biological and process-driven pathways of breakthrough (Levy et al., 2018; Fridey et al., 2020). Simultaneously, the measured deterioration of pH and platelet count across storage reinforces the caution in the platelet PRT literature that extended storage eligibility should not be conflated with preserved *in vivo* function—especially when the evidence base indicates increased activation/apoptosis signals in Mirasol-treated units by late storage (Valsami et al., 2022; Malvaux et al., 2022; Liu et al., 2023).

#### *4.6.5 Plasma coagulation findings: coherent shift in screening markers with persistence after storage*

The plasma findings showed a consistent post-treatment pattern: PT and aPTT prolongation and a marked reduction in fibrinogen, followed by comparatively smaller additional shifts after 30 days frozen storage. This structure mirrors the synthesis in the plasma PRT literature: Mirasol treatment induces measurable reductions in certain coagulation factors (notably fibrinogen and FVIII) and produces modest prolongation of clotting times, while global interpretive frameworks often characterize the residual function as clinically acceptable for many indications (Wasiluk et al., 2020; Rosell-Valle et al., 2022; Sherstyukova et al., 2025; Mokhtarian et al., 2025).

Two analytic points strengthen interpretation. First, the coherence across PT, aPTT, and fibrinogen indicates that the plasma effect is not an isolated assay artifact; rather, it is a consistent directional shift across multiple screening measures. Second, the persistence of the post-treatment profile after frozen storage suggests that the dominant alteration occurs during or immediately after treatment, with storage contributing comparatively less additional drift. This is relevant to clinical operations because it implies that potency reduction—particularly in fibrinogen—should be understood as primarily treatment-associated rather than as a progressive storage degradation over the studied interval.

However, “clinically acceptable” is context-dependent, and the literature explicitly anticipates that high-acuity scenarios requiring maximal factor delivery per unit may be more sensitive to factor reductions (Sherstyukova et al., 2025). The present results therefore support a balanced interpretation: Mirasol-treated plasma retains utility for many

indications, but the hemostatic margin is plausibly reduced, which may matter when dosing constraints exist. This reinforces the broader field motivation to reduce factor loss in next-generation approaches such as visible-light platforms (Stewart et al., 2024).

#### 4.6.6 Operational implications: shelf-life extension benefits are conditional on biological usable life

The operational literature indicates that pathogen reduction can dramatically reduce platelet wastage and improve inventory resilience when it is coupled with shelf-life extension to 7 days and aligned inventory optimization (Gorria et al., 2019; Jimenez-Marco et al., 2018; Fachini et al., 2021; Dillon et al., 2023; Ramirez-Arcos et al., 2020). Conversely, if pathogen reduction does not extend shelf life—or if the biologically “effective usable life” is shortened by quality decline—models predict increased wastage and shortages (Blake et al., 2021; Rebulla & Prati, 2022).

The present platelet indicator trajectories speak directly to this conditionality. While pH stabilized after Day 3, platelet count continued to decline through Day 7, consistent with a pattern of ongoing storage lesion. This does not prove that Day-7 platelets are clinically inferior, but it does support the operational caution present in the literature: there can be a tension between inventory shelf-life (what regulations allow) and biological functional life (what a unit can deliver clinically), especially for riboflavin/UV-treated platelets (Malvaux et al., 2022; Valsami et al., 2022). Therefore, operational arguments for 7-day inventories should remain linked to quality monitoring and clinical-context deployment strategies (e.g., prioritizing fresher units for high-risk bleeding scenarios), rather than assuming uniform equivalence across storage days.

#### 4.6.7 How the findings address the literature gaps

The study’s contribution becomes clearer when mapped directly onto the literature gaps:

- a. Residual risk after PRT: The 9/10 culture-negative outcome supports substantial suppression while the single late-positive treated pool empirically illustrates why PRT reduces but does not eliminate risk (Levy et al., 2018; Friley et al., 2020).
- b. Bounded meaning of “viability”: By demonstrating significant time effects in pH and platelet count, the study provides

clear evidence of measurable degradation while still requiring disciplined avoidance of clinical-function claims absent functional assays (Valsami et al., 2022; Liu et al., 2023).

- c. Context-specific evidence: The results provide a workflow-embedded profile of suppression and quality indicators that is locally informative in the way the literature recommends for platform decisions (Diallo et al., 2020; Malvaux et al., 2022).
- d. Plasma parameter persistence: The pre/post and post-storage structure quantifies that the dominant coagulation shift is treatment-associated and persists through storage (Wasiluk et al., 2020; Sherstyukova et al., 2025).
- e. Inventory alignment: The platelet indicator trends reinforce the operational literature’s conditionality—inventory benefits depend on biological usability and allocation strategy, not merely regulatory shelf-life (Dillon et al., 2023; Blake et al., 2021).

## 5. Conclusions, Recommendations, Study Implications, and Future Directions

### 5.1 Conclusions

This in vitro evaluation indicates that Mirasol pathogen reduction, applied to platelet concentrates challenged with *Staphylococcus aureus* (ATCC 25923), achieved substantial bacterial suppression under the study’s culture-monitoring conditions, with most treated pools remaining culture-negative at Day 7 while a single treated pool demonstrated late culture positivity. In practical terms, the findings support the interpretation of Mirasol PRT as a strong risk-reduction layer rather than an absolute sterilization step, consistent with the broader transfusion-safety framing that platelet-associated bacterial risk is reducible but not fully eliminable.

Concurrently, the platelet storage indicators showed statistically significant time-associated deterioration following treatment and during room-temperature storage. Platelet pH demonstrated an early decline through Day 3 with stabilization



thereafter at the group level, whereas platelet count showed a progressive decline across the entire storage horizon, with the largest separation observed by Day 7. Taken together, these results indicate that while Mirasol PRT supports meaningful bacterial risk mitigation, it is accompanied by measurable storage-associated changes in platelet quality proxies across time. The findings therefore reinforce a central evidence-based perspective in transfusion medicine: pathogen reduction decisions are best interpreted as a safety–quality balance shaped by storage duration and clinical context.

For plasma, Mirasol-treated units demonstrated a coherent pattern of prolonged PT and aPTT and reduced fibrinogen activity immediately after treatment, with these changes persisting after 30 days of frozen storage and only modest additional drift post-storage. These results support the conclusion that Mirasol PRT produces measurable changes in coagulation screening markers while maintaining a stable post-treatment profile through short-term frozen storage, consistent with the view that pathogen reduction may reduce hemostatic potency margins even when overall usability remains intact for many clinical indications.

### 5.2 Recommendations

For platelet components, the results support continued use of Mirasol PRT as an integral safety layer for mitigating bacterial risk, especially in environments where room-temperature platelet storage and distribution logistics heighten exposure to transfusion-transmitted bacterial infection. However, given the observed storage-associated deterioration in platelet indicators—particularly the sustained decline in platelet count through Day 7—inventory management practices should be aligned with a risk–benefit allocation strategy. Where operationally feasible, earlier storage-day units (e.g., Day 0–Day 3) should be prioritized for patient groups with higher bleeding risk or anticipated need for optimal post-transfusion increments, while later storage-day units may be reserved for scenarios where inventory continuity is critical and clinical context permits.

For plasma components, clinicians and transfusion services should recognize that Mirasol PRT is associated with measurable shifts in coagulation screening results (PT/aPTT prolongation and reduced fibrinogen). This warrants an operational posture of dose awareness in settings where maximal factor delivery per unit is clinically

important, particularly in severe coagulopathy with volume restriction. Local transfusion protocols may consider reinforcing guidance that treatment-related potency shifts can occur, while maintaining the use of Mirasol-treated plasma where pathogen reduction benefits are prioritized.

From a systems standpoint, implementation decisions should avoid assuming that shelf-life extension automatically produces operational gains. Instead, wastage reduction and resilience benefits should be treated as conditional on how “usable life” is operationalized and how components are allocated by storage day. Inventory optimization strategies—donor scheduling, production planning, and demand forecasting—should be configured to leverage safety benefits while minimizing reliance on late-storage products when clinical circumstances warrant higher functional margins.

### 5.3 Study implications

The study contributes a tightly linked view of pathogen reduction outcomes across two clinically relevant component types—platelets and plasma—by demonstrating that Mirasol PRT can provide substantial bacterial suppression while producing measurable changes in platelet storage indicators and plasma coagulation parameters. This integrated perspective strengthens professional decision-making by clarifying that pathogen reduction is not a single-axis improvement, but an intervention that shifts risk profiles and quality proxies in parallel. The results underscore the importance of interpreting “viability” and “integrity” within the limits of measured endpoints—here, pH and platelet count for platelets, and PT/aPTT/fibrinogen for plasma—rather than treating regulatory eligibility or numeric thresholds as synonymous with full clinical equivalence across storage days.

In operational terms, the data reinforce the need to connect pathogen reduction policies to inventory management and clinical allocation strategies. The results support the proposition that safety enhancements are maximized when they are integrated into a broader quality system that includes aseptic handling, storage control, and deliberate distribution practices.

### 5.4 Future directions

Future studies should extend the present work in three complementary directions. First, bacterial suppression evaluation can be strengthened by incorporating additional clinically relevant



organisms (including Gram-negative species and spore-forming bacteria), assessing broader challenge conditions, and systematically examining late-positive pathways under prolonged storage scenarios. Second, platelet quality evaluation would benefit from expanding beyond storage indicators to include functional and mechanistic measures—such as swirling assessment, aggregation or hypotonic shock response, activation and apoptosis markers, and extracellular vesicle profiling—to better characterize how storage-day changes translate into functional capacity. Third, plasma evaluation should include broader factor profiling (e.g., FVIII and other labile factors), alongside global hemostasis assays where feasible, to better contextualize screening-test changes within overall clotting capacity.

Finally, translational research that links component-level changes to clinical endpoints—such as post-transfusion increments, bleeding outcomes, and dose requirements—would provide the strongest basis for aligning pathogen reduction policy, shelf-life decisions, and patient-specific allocation strategies.

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7. Tables

**Table 1. pH results before and after MPRT**

Pool Serial #	Before MPRT	After MPRT		
		Day 0	Day 3	Day 7
1	7.15	7.10	6.83	6.82
2	7.15	7.10	6.86	6.85
3	7.14	7.07	6.84	6.73
4	7.22	7.17	6.85	6.62
5	7.21	7.12	6.86	6.86
6	7.25	7.15	6.94	6.82
7	7.22	7.17	6.80	6.80
8	7.28	7.22	6.83	7.22
9	7.22	7.20	6.81	6.80
10	7.20	7.12	6.77	6.77
Mean	7.20	7.10	6.80	6.80

**Table 2. Comparison of pH values before and after MPRT treatment**

	Mean	F value	p-value	Interpretation
Before MPRT	7.204	64.239	0.000	Significant
Day 0	7.142	64.239	0.000	Significant
Day 3	6.839	64.239	0.000	Significant
Day 7	6.829	64.239	0.000	Significant

*Sig. p=0.05*

**Table 3. Pairwise comparison of pH values before and after MPRT treatment**

	Time	p-value	Interpretation
Before MPRT	Day 0	0.000	Significant
	Day 3	0.000	Significant
	Day 7	0.000	Significant
Day 0	Before	0.000	Significant
	Day 3	0.000	Significant
	Day 7	0.000	Significant
Day 3	Before	0.000	Significant
	Day 0	0.000	Significant
	Day 7	1.000	Not Significant
Day 7	Before	0.000	Significant
	Day 0	0.000	Significant
	Day 3	1.000	Not Significant

*Sig. p=0.05*

**Table 4. Platelet count determination ( $10^3/\text{ul}$ ) before and after MPRT treatment**

Pool Serial #	Before MPRT Treatment	After MPRT Treatment		
		Day 0	Day 3	Day 7
1	1239	1274	1164	957
2	1517	1365	1107	956
3	1278	1201	1087	847
4	1565	1384	1388	820
5	1202	1027	968	835
6	924	868	828	683
7	1380	1237	1188	862
8	994	905	876	820
9	1372	1332	1279	935
10	1495	1397	1323	1079
Mean	1296.6	1199	1120	879.4

**Table 5. Comparison of platelet count before and after MPRT treatment**

	Mean	F value	p-value	Interpretation
Before MPRT	1296.6	43.958	0.000	Significant
Day 0	1199	43.958	0.000	Significant
Day 3	1120.8	43.958	0.000	Significant
Day 7	879.4	43.958	0.000	Significant

*Sig. p=0.05*

**Table 6. Pairwise comparison of platelet count before and after MPRT treatment**

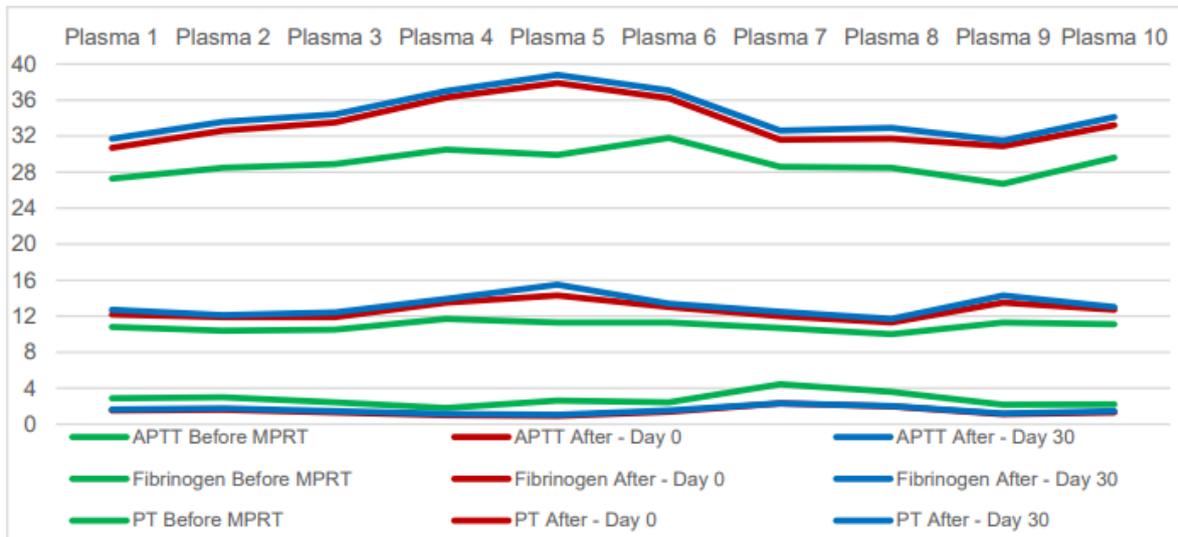
	Time	p-value	Interpretation
Before MPRT	Day 0	0.008	Significant
	Day 3	0.002	Significant
	Day 7	0.000	Significant
Day 0	Before	0.008	Significant
	Day 3	0.046	Significant
	Day 7	0.000	Significant
Day 3	Before	0.002	Significant
	Day 0	0.046	Significant
	Day 7	0.003	Significant
Day 7	Before	0.000	Significant
	Day 0	0.000	Significant
	Day 3	0.003	Significant

*Sig. p=0.05*

**Table 7. Results of Bacterial Culture**

Pool Serial#	NC after 7 days	PC after 24 hours	PC after 7 days	MT after 7 days	Remarks
1	-	+	+	-	Valid
2	-	+	+	-	Valid
3	-	+	+	-	Valid
4	-	+	+	+	Failed
5	-	+	+	-	Valid
6	-	+	+	-	Valid
7	-	+	+	-	Valid
8	-	+	+	-	Valid
9	-	+	+	-	Valid
10	-	+	+	-	Valid

Legend: NC: Negative Control, PC: Positive Control, MT: MPRT-treated



**Figure 1.** APTT, Fibrinogen and PT before MPRT, After – Day 0, and After – Day 30

**Table 8. Coagulation Factor determination in Plasma**

Plasma #	PT (sec)			aPTT (sec)			Fibrinogen (g/L)		
	Before MPRT	After MPRT		Before MPRT	After MPRT		Before MPRT	After MPRT	
		Day 0	Day 30		Day 0	Day 30		Day 0	Day 30
1	10.8	12.2	12.7	27.3	30.7	31.7	2.88	1.54	1.65
2	10.4	11.9	12.1	28.5	32.6	33.6	2.98	1.60	1.76
3	10.5	11.9	12.4	28.9	33.5	34.4	2.44	1.30	1.47
4	11.7	13.5	13.9	30.5	36.3	37.0	1.80	0.99	1.15
5	11.3	14.3	15.5	29.9	37.9	38.8	2.61	0.92	1.05
6	11.3	13.0	13.4	31.8	36.2	37.1	2.44	1.38	1.51
7	10.7	12.0	12.5	28.6	31.6	32.6	4.44	2.31	2.32
8	10.0	11.3	11.7	28.5	31.7	32.9	3.61	1.97	2.01
9	11.3	13.5	14.3	26.7	30.9	31.5	2.15	1.13	1.18
10	11.1	12.7	13.0	29.6	33.2	34.1	2.21	1.31	1.45
Mean	10.91	12.63	13.15	29.03	33.46	34.37	2.76	1.45	1.56

**Table 9. Descriptive Statistics for Coagulation Factors**

	PT (sec)			aPTT (sec)			Fibrinogen (g/L)		
	Before	Day 0	Day 30	Before	Day 0	Day 30	Before	Day 0	Day 30
Mean	10.91	12.63	13.15	29.03	33.46	34.37	2.756	1.445	1.555
F-value	84.377			112.96			84.846		
p-value	0.000			0.000			0.000		
Interpretation	Significant			Significant			Significant		

**Table 10. Pairwise comparison of Coagulation Factors before and after MPRT treatment**

Time	PT p-value	Interpretation	aPTT p-value	Interpretation	Fibrinogen p-value	Interpretation	
Before MPRT	Day 0	0.000	Significant	0.000	Significant	0.000	Significant
	Day 30	0.000	Significant	0.000	Significant	0.000	Significant
Day 0	Before	0.000	Significant	0.000	Significant	0.000	Significant
	Day 30	0.000	Significant	0.000	Significant	0.001	Significant
Day 30	Before	0.000	Significant	0.000	Significant	0.000	Significant
	Day 0	0.000	Significant	0.000	Significant	0.001	Significant

Sig.  $p=0.05$