Cryopreserved Platelets Can Be Rapidly Thawed in Under 8 Minutes and Are Compatible with Water-Bath and Dry Plasma Thawers (MHSRS-25-14198)

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INTRODUCTION

CLPH-511 is a frozen platelet product formulated with 6% dimethyl sulfoxide (DMSO) and a freezing volume of 20-35 mL. CLPH-511 is manufactured in batches using irradiated, apheresis platelets (≤12 units from ≤10 type O+/- donors). Platelets are concentrated via centrifugation, pooled, formulated to 6% DMSO, filled into cryobags, and frozen/stored at ≤-65°C. Frozen CLPH-511 is stable for 5 years and thawed CLPH-511 is stable for up to 8 hours at room temperature.

CLPH-511 is being developed as a potential alternative to standard platelets for treatment of acute hemorrhage. The phase 2/3 clinical trial (NCT04709705) was completed early at the interim analysis after reaching the pre-specified efficacy requirement for statistical non-inferiority.

Currently, only water-bath thawers are used to thaw CLPH-511. This study explores CLPH-511's compatibility with two types of dry plasma thawers. Dry thawers may be advantageous in scenarios where a water bath is cumbersome and/or where power-supply is limited, such as on a ship or in other far-forward environments.

MATERIALS AND METHODS

The ZipThaw® (FreMon Scientific) and SAHARA-III (SARSTEDT) dry thawers were evaluated using CLPH-511, and the QuickThaw® DH8 (Helmer Scientific) was used as a control group for water-bath plasma thawers (n = 3 units per thawer from 3 lots, 1 unit/lot/thawer). All 3 thawers are FDA cleared devices for warming blood and plasma.

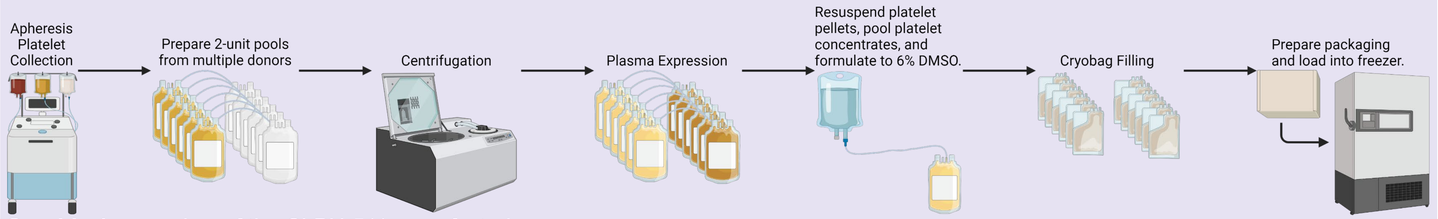
After 3.5 years of storage, the CLPH-511 units were thawed at ~37°C until they reached ≥30°C and then 25 mL saline was added. The units were visually inspected (for bag integrity, aggregates, and swirling) and tested for platelet count, pH, thrombin generation (TGA), $CD61^+$ microparticle count (≤ 0.5 µm), and lactadherin positivity.

For the QuickThaw® and SAHARA-III the CLPH-511 units were thawed using a constant duration of 5 and 7.5 minutes, respectively. For the ZipThaw® the thaw times varied (4-5 minutes) based on the thawer's product temperature sensor.

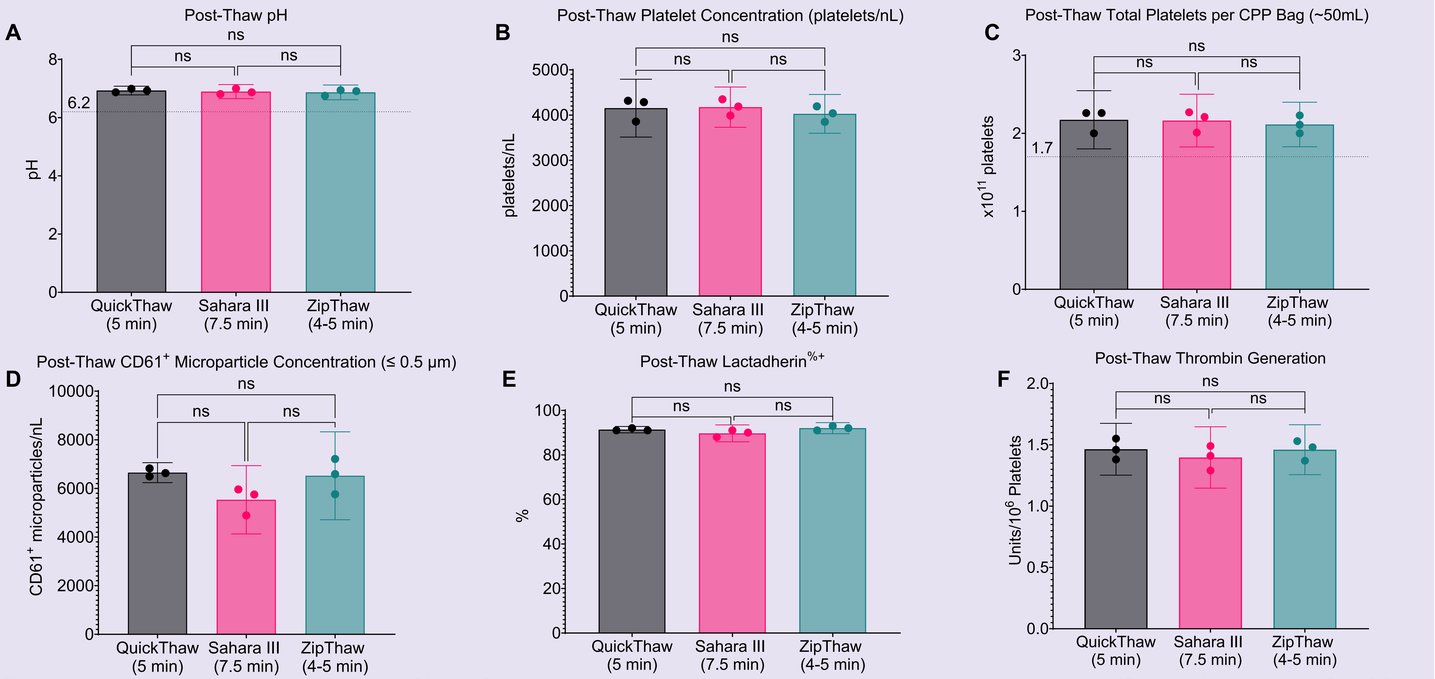
RESULTS

Graphic 1:

Pooled Cryopreserved Platelet Process



Graphic 1 - overview of the CLPH-511 manufacturing process.



For each thawer, the mean +/- the 95% confidence interval is shown for pH (**A**), platelet concentration (**B**), total platelets (**C**), $CD61^+$ microparticle concentration (**D**), lactadherin % positive (**E**), and thrombin generation (**F**). For pH and total platelets, the release specifications are denoted by the dotted lines (pH ≥6.2 and ≥$1.7x10^{11}$ total platelets). Statistics presented for one-way ANOVA: ns is $p>0.05$. Upon visual inspection all bags were intact (leak free), swirling was observed, and no aggregates were observed.

QuickThaw® DH8:

ZipThaw®:

SAHARA-III:

AIMS

1) Describe that CLPH-511 can be thawed quickly (≤7.5 minutes).
2) Understand that thawing CLPH-511 is feasible with water-bath and dry plasma thawers.
3) Discuss which thawing methods are most applicable for certain situations and the potential practical advantages of CLPH-511.

CONCLUSION

The thaw times for the QuickThaw®, ZipThaw®, and SAHARA III were 5, 4-5, and 7.5 minutes, respectively, with average post-thaw temperatures of 35, 32, and 34°C, when measured with an infrared temperature probe. For the SAHARA-III a constant duration had to be used since the thawer's product temperature sensor did not function properly with CLPH-511, likely due to CLPH-511's small volume relative to the blood components that the SARAHA-III was designed for (whole blood, red cell, and plasma units).

All CLPH-511 units met the release criteria for pH (≥6.2), total platelets (≥$1.7x10^{11}$ platelets), and visual inspection (aggregate-free swirling and leak-free). In addition, the characterization testing for TGA (potency), CD61+ microparticle count (purity), and lactadherin positivity (identity) was consistent with historical CLPH-511 data (n=93 batches). No significant differences were observed in the analytical data between the three thawers ($p>0.05$, ordinary one-way ANOVA).

CLPH-511 appears to be compatible with multiple thawing technologies and has a small volume that thaws quickly (≤7.5 minutes), this makes CLPH-511 potentially well-suited for emergency situations and/or field environments without a water bath. Additional thawing validation studies are needed prior to clinical use of CLPH-511 with dry thawers.

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