Supplemental Information for Hospitals Participating in the MIPLATE Clinical Trial

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1 Background

1.1 Pathogen Reduction

Pathogen Reduction is an approach for the prevention of transfusion-transmitted diseases that is both proactive and broad-spectrum. It is proactive because it could remove the necessity of developing specific assays for emerging pathogens and it is considered broad-spectrum because it has the potential to reduce the load of viruses, parasites, and bacteria (exclusive of prions) that may be present in a blood component. Pathogen Reduction is not a new concept as it has been successfully used in the plasma fractionation industry for years e.g.: Low pH, pasteurization, solvent detergent, nanofiltration, etc. More recently, Pathogen Reduction technologies have been developed to treat plasma and platelets for transfusion.

1.2 MIPLATE Clinical Trial

The MIPLATE clinical trial is designed to demonstrate the clinical hemostatic efficacy of Mirasol-treated apheresis platelets compared to standard of care apheresis platelets in hematology oncology patients with treatment-induced thrombocytopenia.

1.3 Mirasol® Pathogen Reduction Technology

The Mirasol System developed by Terumo BCT is intended for pathogen reduction and inactivation of residual white blood cells in blood components. It uses riboflavin (vitamin B2) in conjunction with UV light to induce irreversible damages to the nucleic acids (DNA & RNA) in all the cells, parasites, bacteria and viruses (not prions) of the blood component mixture. Consequently, the ability of pathogens to replicate is reduced, minimizing the potential for disease transmission to the patient receiving the Mirasol-treated apheresis platelet.

2 Characteristics of the Mirasol-treated Platelet

The Mirasol-treated apheresis platelet product will be produced at the Bloodworks Northwest (BWNW) production site. It will be produced separately from the standard of care apheresis platelets as it is not a licensed product. **Because Mirasol-treated apheresis platelets will be created on an as needed basis, routine communications between the blood center and transfusion centers will be needed to ensure product availability of the correct blood type for the anticipated demand**.

3 Storage Requirements of the Mirasol-treated Platelet

Unlike the standard of care apheresis platelets product, the Mirasol-treated apheresis platelets are light sensitive. From the time of receipt until the time of transfusion, protect the Mirasol-treated apheresis platelet product from prolonged exposure to direct sunlight or strong ambient light sources. To ensure sufficient protection from light, store the Mirasol-treated apheresis platelet product in an enclosed platelet storage cabinet or on any intermediate shelf of an open tabletop platelet agitator. Do not store the platelet product on the top shelf of an open tabletop platelet agitator where it will be exposed to direct ambient light or sunlight.

Store until the expiration date and time found on the label at 20 - 24°C with gentle agitation out of direct ambient light or sunlight.

4 Labeling of the Mirasol-treated Platelet

This Mirasol-treated apheresis platelet product will bear an ISBT 128 compliant label. Examples of non-irradiated and irradiated platelet labels are below.

4.1 Label for Mirasol-treated apheresis platelet – Not Irradiated

The Product (Component) Code for this product is: E5748V00.

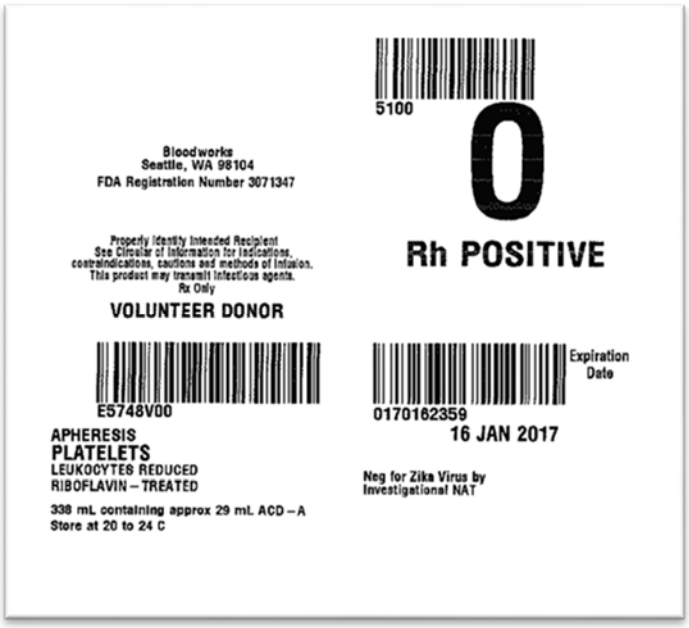


Figure 1: Label of a Mirasol-treated apheresis platelet – Not Irradiated

4.2 Label for Mirasol-treated apheresis platelet – Irradiated

The Product (Component) Code for this product is: E5756V00.

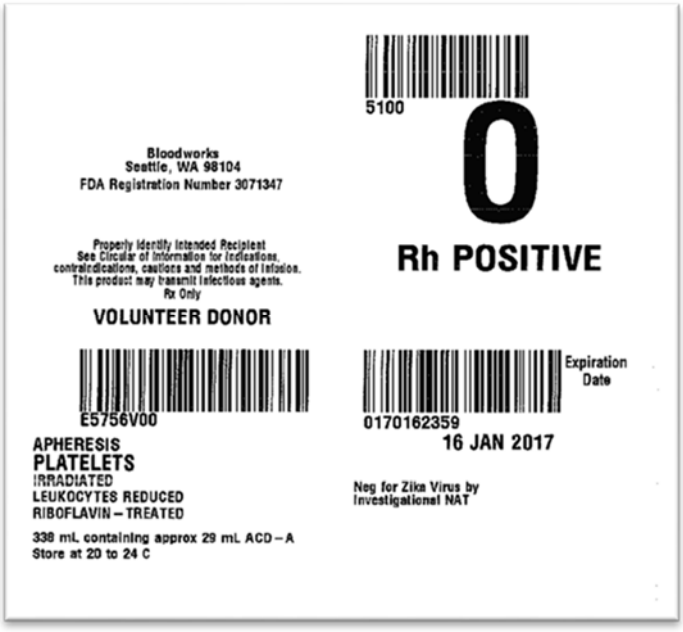
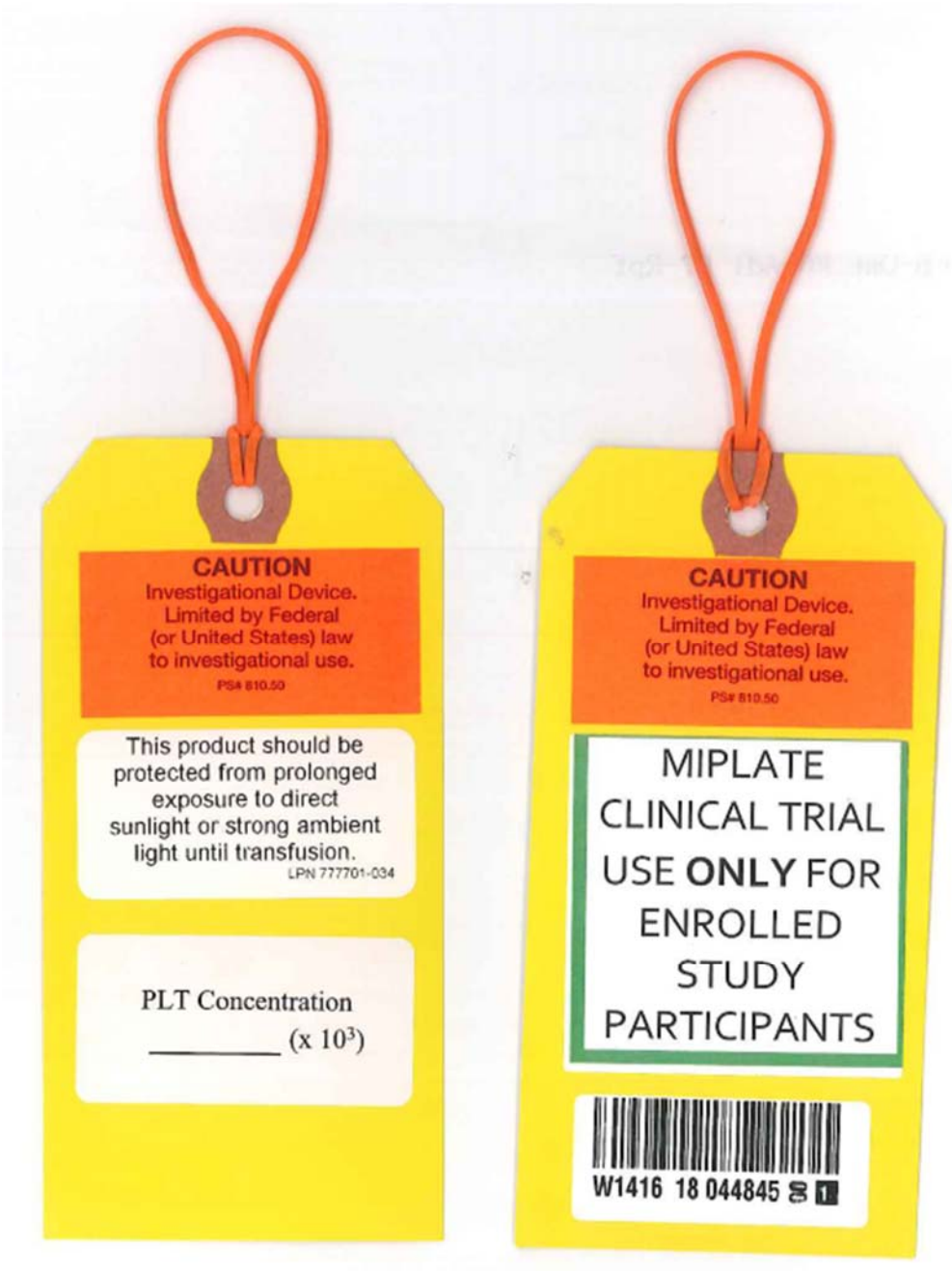


Figure 2: Label of a Mirasol-treated apheresis platelet – Irradiated

4.3 Tie tag for Mirasol-treated apheresis platelet

In addition to the label, **a bright yellow tie tag** will be attached to every Mirasol-treated apheresis platelet. This tag will bear the unit ID, platelet concentration, Investigational statement and instructions to protect product from light. The use of the tag is necessary due to the limited available space on the Product Label. Figure 3 below shows a representation of the tag.



Front of tag Back of tag

Figure 3: Tie tag

5 Mirasol-treated product (component) codes

The Mirasol-treated apheresis platelet and the Mirasol-treated apheresis platelet - Irradiated have been assigned new product (component) codes. These ordering codes are currently in BloodHub.

Other participating hospitals will need to update their information systems to include these new product (component) codes. See Table 1 below.

Table 1: Product (Component) codes

• **Single Mirasol-treated apheresis platelet – Not Irradiated**	**E5748V00**
• **Single Mirasol-treated apheresis platelet – Irradiated**	**E5756V00**
• **Container 1: Mirasol-treated apheresis platelet – Not Irradiated**	**E5749V00**
• **Container 2: Mirasol-treated apheresis platelet – Not Irradiated**	**E5750V00**
• **Container 3: Mirasol-treated apheresis platelet – Not Irradiated**	**E5751V00**
• **Container 1: Mirasol-treated apheresis platelet – Irradiated**	**E5757V00**
• **Container 2: Mirasol-treated apheresis platelet – Irradiated**	**E5758V00**
• **Container 3: Mirasol-treated apheresis platelet – Irradiated**	**E5759V00**

6 Ordering Platelet products for the MIPLATE study

Control arm apheresis platelets (i.e. current standard of care apheresis platelets) are to be ordered through your local blood supplier as per standard hospital procedures.

Mirasol-treated apheresis platelets are to be ordered through BWNW using the **CTS-5030: MIPLATE Study PLT Order Form** (See Appendix A).

Important Note: Production of the Mirasol-treated product will require regular communication about up-coming patient enrollment and the expected transfusion dates of enrolled patients. The sharing of this information will be a key element in assisting BWNW to meet the specific study patient's platelet need and to be able to delivery units in a timely manner. **Mirasol-treated platelet units will be made only on demand for a specific study subject.**

Please consider your need for CMV negative or HLA matched product before placing your order. Orders with specific requirements will require more lead time for donor recruitment in order to ensure product

availability.

Mirasol-treated Platelets Ordering Steps:

1. Complete MIPLATE Study PLT Order Form
2. Email order directly to: MIPLATE BWNW Notification Group

   MIPLATEBWNW@bloodworksnw.org
3. Enter order in BloodHub and attach signed MIPLATE Study PLT Order Form
4. Place the original signed order form in the MIPLATE Subject Order Form Binder.

6.1 MIPLATE clinical trial ordering timelines

Order Mirasol-treated apheresis platelets using the study specific order form that has been created: **MIPLATE Study PLT Order Form** (see Appendix A). Please make sure to complete the expected date of transfusion as indicated in the allocated space.

Questions call: **BWNW Hospital Services - 425-656-3081**

Products will be shipped to arrive early morning or early evening and be available for transfusion over the 4 day viability period shown in Figure 4 on next page.

Platelet collections for Mirasol-treated units are performed 7 days a week. See Figure 4 for timeline of ordering and expected release dates on next page.

6.1.1 Timelines for routine orders/transfusion days of Mirasol-treated apheresis platelets

SUNDAY	MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY	SATURDAY
Collection Day 0	Treatment/Testing Day 1	Release from BWNW Early Morning Day 2	Available for Tx Day 3	Available for Tx Day 4	Available for Tx Day 5. Expiration at midnight – send unit back to BWNW	
	Release from BWNW Evening Day 1 or **TUES AM**	Available for Tx Day 2				

SUNDAY	**MONDAY**	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY	SATURDAY
	Collection Day 0	Treatment/Testing Day 1	Release from BWNW Early Morning Day 2	Available for Tx Day 3	Available for Tx Day 4	Available for Tx Day 5.Expiration at midnight - send unit back to BWNW
		Release from BWNW Evening Day 1 or **WED AM**	Available for Tx Day 2			

SUNDAY	MONDAY	**TUESDAY**	WEDNESDAY	THURSDAY	FRIDAY	SATURDAY
Available for Tx Day 5. Expiration at midnight – send unit back to BWNW		Collection Day 0	Treatment/Testing Day 1	Release from BWNW Early Morning Day 2	Available for Tx Day 3	Available for Tx Day 4
			Release from BWNW Evening Day 1 or **THURS AM**	Available for Tx Day 2		

SUNDAY	MONDAY	TUESDAY	**WEDNESDAY**	THURSDAY	FRIDAY	SATURDAY
Available for Tx Day 4	Available for Tx Day 5. Expiration at midnight – send unit back to BWNW		Collection Day 0	Treatment/Testing Day 1	Release from BWNW Early Morning Day 2	Available for Tx Day 3
				Release from BWNW Evening Day 1 or **FRI AM**	Available for Tx Day 2	

SUNDAY	MONDAY	TUESDAY	WEDNESDAY	**THURSDAY**	FRIDAY	SATURDAY
Available for Tx Day 3	Available for Tx Day 4	Available for Tx Day 5.Expiration at midnight - send unit back to BWNW		Collection Day 0	Treatment/Testing Day 1	Release from BWNW Early Morning Day 2
					Release from BWNW Evening Day 1 or **SAT AM**	Available for Tx Day 2

SUNDAY	MONDAY	TUESDAY	WEDNESDAY	THURSDAY	**FRIDAY**	SATURDAY
Release from BWNW Early Morning Day 2	Available for Tx Day 3	Available for Tx Day 4	Available for Tx Day 5. Expiration at midnight - send unit back to BWNW		Collection Day 0	Treatment/Testing Day 1
Available for Tx Day 2						Release from BWNW Evening Day 1 or **SUN AM**

SUNDAY	MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY	**SATURDAY**
Treatment/Testing Day 1	Release from BWNW Early Morning Day 2	Available for Tx Day 3	Available for Tx Day 4	Available for Tx Day 5. Expiration at midnight - send unit back to BWNW		Collection Day 0
Release from BWNW Evening Day 1 or **MON AM**	Available for Tx Day 2					

Orange Boxes = At BWNW Collection, Testing or No Action Days **Green Boxes** = At Hospital product available for Transfusion (Tx)

Figure 4: Timelines for routine orders showing collection, treatment, release and product availability days.

6.1.2 For urgent orders of Mirasol-treated apheresis platelets (STAT Order).

STAT Orders must be entered in BloodHub. Call BWNW Hospital Service to confirm 'STAT' status. Availability of product may be limited to actual collected apheresis units and time allowance for processing and final testing prior to issuing.

BWNW Hospital Services - 425-656-3081

6.2 Delivery mode for Mirasol-treated apheresis platelet

The Mirasol-treated apheresis platelet products will be shipped to the participating hospitals using BWNW established courier service.

7 Administering Platelet Products

Mirasol-treated apheresis platelets may **ONLY** be provided to patients enrolled in the clinical trial and should be administered with the same care as any other platelet product while also complying with the MIPLATE protocol.

Important Note: See Appendix B for information on appearance of platelet unit - color and broken frangibile.

The color of the product and urine of recipient may have a yellow coloring which is a known side effect of the riboflavin used in the processing of the platelets.

Broken parts of the frangible connectors will be present in the Mirasol-treated apheresis platelet storage bag. This is a normal part of the manufacturing process and will not interfere with the transfusion. The broken parts of the frangible connectors will remain in the bag before and after transfusion of the platelet product.

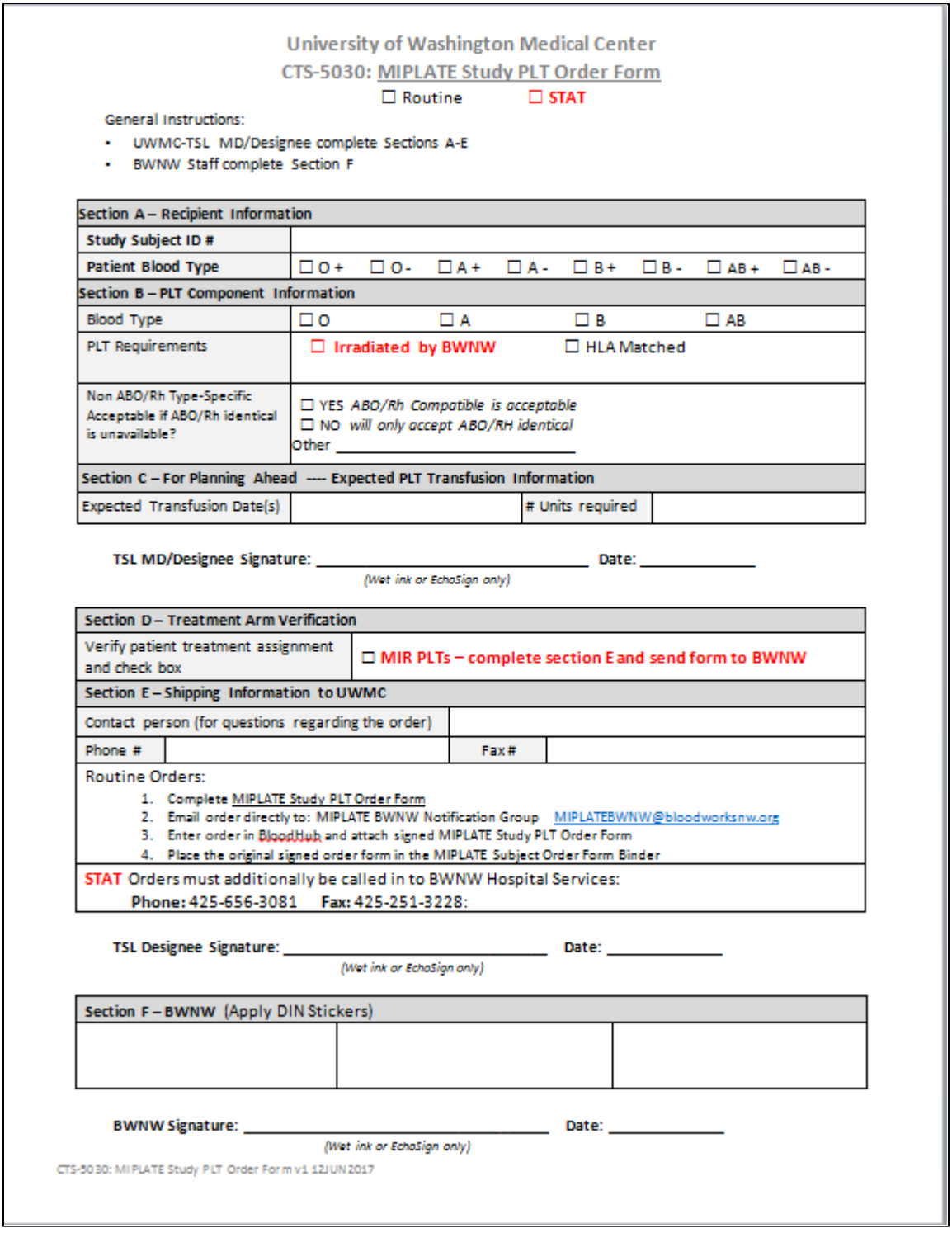
8 Adverse Event Reporting

Please report ALL adverse transfusion events transpiring within the study, including events surrounding test and control arm platelets, as per the MIPLATE protocol.

9 Returning and Final Disposition of Mirasol-treated apheresis platelet units.

All unused Mirasol-treated platelet products must be returned to BWNW. Follow UWMC-TSL-Returning Products SOP. Returned products will be credited on next billing cycle.

Appendix A – CTS-5030: MIPLATE Study PLT Order Form



University of Washington Medical Center

CTS-5030: MIPLATE Study PLT Order Form

☐ Routine ☐ STAT

General Instructions:

- UWMC-TSL MD/Designee complete Sections A-E
- BWNW Staff complete Section F

Section A – Recipient Information								
Study Subject ID #								
Patient Blood Type	☐ O +	☐ O -	☐ A +	☐ A -	☐ B +	☐ B -	☐ AB +	☐ AB -
Section B – PLT Component Information								
Blood Type	☐ O	☐ A	☐ B	☐ AB				
PLT Requirements	☐ Irradiated by BWNW	☐ HLA Matched						
Non ABO/Rh Type-Specific Acceptable if ABO/Rh identical is unavailable?	☐ YES *ABO/Rh Compatible is acceptable* ☐ NO *will only accept ABO/RH identical* Other _____							
Section C – For Planning Ahead ---- Expected PLT Transfusion Information								
Expected Transfusion Date(s)		# Units required						

TSL MD/Designee Signature: _____ **Date:** _____

(Wet ink or EchoSign only)

Section D – Treatment Arm Verification	
Verify patient treatment assignment and check box	☐ MIR PLTs – complete section E and send form to BWNW
Section E – Shipping Information to UWMC	
Contact person (for questions regarding the order)	
Phone #	Fax #
Routine Orders: 1. Complete MIPLATE Study PLT Order Form 2. Email order directly to: MIPLATE BWNW Notification Group MIPLATEBWNW@bloodworksnw.org 3. Enter order in BloodHub and attach signed MIPLATE Study PLT Order Form 4. Place the original signed order form in the MIPLATE Subject Order Form Binder	
STAT Orders must additionally be called in to BWNW Hospital Services: **Phone:** 425-656-3081 **Fax:** 425-251-3228:	

TSL Designee Signature: _____ **Date:** _____

(Wet ink or EchoSign only)

Section F – BWNW (Apply DIN Stickers)		

BWNW Signature: _____ **Date:** _____

(Wet ink or EchoSign only)

CTS-5030: MIPLATE Study PLT Order Form v1 12JUN2017

Form provided for information only. The final version of the ordering form will be made available to participating hospitals prior to the initiation of the clinical trial.

Appendix B – MIPLATE Unit Picture to Show Color and Broken Frangible

Color: Mirasol-treated platelet products and the urine of Mirasol-treated transfusion recipients may have a yellow coloring which is a known side effect of the riboflavin used in the processing.

Broken Frangible: In the last step of the Mirasol treatment process and an important item for the transfusion and care staff to be aware of is the presence of a broken frangible in the platelet bag. The frangibles were purposefully isolated in this picture so they can be clearly seen. They will typically be free floating in the platelets and not easily seen, but they will occasionally be visible when near the side of the bag.