



**Operator's Manual
And
Instructions for Use
HDL Therapeutics, Inc.
Plasma Delipidation System (PDS-2™ System)**



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CAUTION: Federal law restricts this device to sale by or on the order of a physician. Humanitarian Device. Authorized by Federal law for use in the treatment of Homozygous Familial Hypercholesterolemia (HoFH). The effectiveness of this device for this use has not been demonstrated.

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1. Indications for Use

The Plasma Delipidation System (PDS-2™ System) is indicated to reduce coronary artery atheroma in adult patients with Homozygous Familial Hypercholesterolemia (HoFH) who are either inadequately responsive to or intolerant of maximal therapy for HoFH, including the latest medications and other device therapies approved by the FDA.

2. Contraindications

Standard contraindications related to plasmapheresis and plasmapheresis systems including:

- Patients who are in an actively septic state or are hemodynamically unstable
- Patients with heparin allergies should not receive heparin as an anticoagulant during plasmapheresis
- Patients with persistent hypocalcemia are at risk for worsening of their conditions because citrate is commonly used to prevent clotting and can potentiate hypocalcemia

Following are contraindications for the PDS-2 System:

- Patients with a known hyper-coagulable condition manifesting in history of highly suspected deep venous thrombosis or pulmonary embolism
- Patients with active cholecystitis
- Patients with unstable or uncontrolled hypertension
- Patients with unstable or uncontrolled insulin dependent diabetics

3. Warnings

Setup and Credentials

- THIS SYSTEM SHOULD BE OPERATED BY AND SERVICED BY TRAINED PERSONNEL ONLY. IF THE SYSTEM IS OPERATED BY PERSONNEL NOT TRAINED BY HDL THERAPEUTICS, DISCARD THE MATERIALS IN PROCESS OR THE OUTPUT PLASMA PRIOR TO ADMINISTRATION TO A PATIENT.
- THE PDS-2 MUST BE EMPLOYED IN ACCORDANCE WITH THE INSTRUCTIONS FOR USE. IN THE EVENT THE SYSTEM IS OPERATED INCORRECTLY, DISCARD THE MATERIALS IN PROCESS OR THE OUTPUT PLASMA PRIOR TO ADMINISTRATION TO A PATIENT.

Patient Conditions

- INQUIRE ABOUT THE USE OF IMPLANTABLE OR OTHER MEDICAL DEVICES (E.G., PACEMAKERS, NERVE STIMULATORS, INFUSION PUMP) AND POSSIBLE INTERFERENCE WITH THE HDL THERAPEUTICS DEVICE SYSTEM. IF THE PATIENT HAS AN IMPLANTABLE MEDICAL DEVICE OR USES A DEVICE THAT MAY INTERFERE WITH THE PDS-2 SYSTEM, DO NOT PROCEED WITH TREATMENT.
- THERAPY SESSION WITH THE PDS-2 SYSTEM IS LIMITED TO SEVEN, WEEKLY TREATMENTS. IN THE EVENT THAT A THERAPY SESSION EXCEEDS THE SEVEN WEEKLY TREATMENTS, MONITOR THE PATIENT APPROPRIATELY.
- THE THERAPY COULD POTENTIALLY CAUSE A FLUID IMBALANCE DURING THE PROCEDURE. IF THE PATIENT EXHIBITS A FLUID IMBALANCE DURING TREATMENT, MONITOR CLOSELY AND APPLY APPROPRIATE MEDICAL TREATMENT AS NEEDED.
- PATIENTS WITH IMPAIRED OR ABNORMAL CITRATE METABOLISM (E.G., LIVER DISEASE) MAY DISPLAY CITRATE SENSITIVITY. IF THE PATIENT EXHIBITS CITRATE SENSITIVITY DURING TREATMENT, MONITOR CLOSELY AND APPLY APPROPRIATE MEDICAL TREATMENT AS NEEDED.
- FLUIDS USED DURING TREATMENT SHOULD BE AT ROOM TEMPERATURE TO OPTIMIZE PATIENT COMFORT AND STABLE BLOOD PRESSURE. IF FLUIDS ARE NOT AT ROOM TEMPERATURE, MONITOR BLOOD PRESSURE CLOSELY AND APPLY APPROPRIATE MEDICAL TREATMENT AS NEEDED.

Operation

- IN THE EVENT OF ERROR MESSAGES THAT ARE UNRECOVERABLE OR THE SYSTEM BECOMES NON-RESPONSIVE, DISCARD THE MATERIALS IN PROCESS AND TERMINATE THE DELIPIDATION PROCESS, ENSURING THAT PLASMA THAT MAY CONTAIN EXCESSIVE SOLVENT IS NOT RETURNED TO THE PATIENT. SEE PAGE 43 FOR ADDITIONAL INFORMATION.
- USE PLASMA OBTAINED USING STANDARD PLASMAPHERESIS PROCEDURES, TYPICALLY CITRATED PLASMA. IF NON-STANDARD PLASMAPHERESIS PROCEDURES ARE USED, DISCARD THE MATERIALS IN PROCESS. NOTE: DATA ON THE USE OF HEPARINIZED BLOOD WITH THE DEVICE HAS NOT BEEN COLLECTED AND IT IS UNCLEAR HOW HEPARINIZED BLOOD WILL AFFECT PATIENT OUTCOMES.

- THIS EQUIPMENT SHOULD NOT BE OPERATED IN THE PRESENCE OF FLAMMABLE MIXTURES. IF FLAMMABLE MIXTURES ARE PRESENT, REMOVE THEM BEFORE OPERATING THE PDS-2.
- SHOULD A SPILL OF UNTREATED PLASMA, TREATED PLASMA, OR SOLVENT OCCUR, CLEAN AND DISPOSE OF THE SPILL AS REQUIRED BY THE INSTITUTION'S CHEMICAL AND/OR BIOHAZARD PROCEDURES. DISPOSE OF ANY DISPOSABLES, SOLUTIONS, OR PLASMA IF STERILITY HAS BEEN COMPROMISED OR MAY HAVE BEEN COMPROMISED.

Maintenance

- DO NOT USE THE DISPOSABLE TUBING SET IF STERILITY HAS BEEN COMPROMISED.
- DISCARD THE OUTPUT PLASMA IF STERILITY IS NOT MAINTAINED THROUGHOUT THE PROCEDURE.
- DEVICE COMPONENTS SHOULD BE CLEANED AND DISINFECTED USING DISINFECTING WIPES FOLLOWING INSTRUCTIONS PROVIDED IN **SECTION 17 – CARE AND MAINTENANCE**. IF THE DEVICE COMPONENTS ARE NOT CLEANED AND DISINFECTION, OR ARE CLEANED AND DISINFECTED IMPROPERLY, DO NOT OPERATE THE DEVICE UNTIL THE CORRECT CLEANING AND DISINFECTION PROCEDURES ARE VERIFIED BY TRAINED PERSONNEL.

4. Precautions

- DO NOT USE OPERATING OR MAINTENANCE PROCEDURES OTHER THAN THOSE PUBLISHED BY HDL THERAPEUTICS, OR USE ACCESSORY DEVICES NOT RECOMMENDED BY HDL THERAPEUTICS.
 - Only use procedures specified by HDL Therapeutics to operate, maintain, and calibrate the PDS-2.
 - Persons performing the procedures must be appropriately trained and qualified.
 - Any equipment modifications must be performed by qualified persons and be approved in writing by HDL Therapeutics.
 - All electrical installations must comply with all applicable local electrical codes and HDL Therapeutics specifications. USE ONLY ELECTRICAL CABLES SUPPLIED WITH THE SYSTEM
- THE PLASMA DELIPIDATION SETS, SOLVENT-IN BAGS, AND SOLVENT TRANSFER SETS, ARE GAMMA STERILIZED. THE TUBING SETS AND BAGS ARE INTENDED FOR SINGLE USE ONLY. DO NOT REUSE OR RESTERILIZE.

- TRAINED HDL THERAPEUTICS PERSONNEL SHOULD BE PRESENT TO OBSERVE THE ENTIRE DELIPIDATION PROCEDURE.
- PERSONNEL SHOULD CLEARLY UNDERSTAND THE PROPER STEPS TO EXAMINE THAT THE EQUIPMENT IS CORRECTLY FUNCTIONING PRIOR TO OPERATION.
- EXAMINE THE EQUIPMENT PRIOR TO USE TO ENSURE CORRECT OPERATION.
- DO NOT DISTURB THE LOAD CELLS, MIXING PLATFORM, OR PUMP DURING OPERATION.
- THE EQUIPMENT OR SYSTEM SHOULD NOT BE USED ADJACENT TO OR STACKED WITH OTHER EQUIPMENT AND THAT IF ADJACENT OR STACKED USE IS NECESSARY, THE EQUIPMENT OR SYSTEM SHOULD BE OBSERVED TO VERIFY NORMAL OPERATION IN THE CONFIGURATION IN WHICH IT WILL BE USED.
- IF MOISTURE IS DETECTED ON THE SURFACE OF THE TUBING OR ANY OTHER DEVICE COMPONENT, THE DELIPIDATION TECHNICIAN SHOULD RULE OUT A LEAK. IF NO LEAK, CONTINUE. IF A LEAK IS DETECTED, ABORT THE DELIPIDATION SESSION.
- SYSTEM CAN BE USED WITH PATIENTS RECEIVING ELECTROCARDIOGRAM MONITORING.
- THE FLUID PATHWAY OF THE TUBING SET IS STERILE AND NONPYROGENIC. DO NOT USE TUBING SET IF THE END CAPS ARE NOT IN PLACE WHEN OPENED.
- DO NOT USE ALTERNATE POWER PLUGS OR ADAPTERS THAT DISCONNECT THE GREEN WIRE SAFETY GROUND, AND CONNECT NO ITEMS WHICH ARE NOT SPECIFIED.
- USE ONLY THE DISPOSABLE TUBING SET, BAGS, CONSUMABLES, AND ANCILIARY MATERIALS PROVIDED FOR THIS DEVICE BY HDL THERAPEUTICS. CONFIRM PART DESIGNATIONS ON DISPOSABLES LABELS.
- OBSERVE ALL LABELING INSTRUCTIONS ON THE PDS-2, DISPOSABLES AND CONSUMABLES.
- DO NOT CONNECT THE INPUT/OUTPUT CABLING AND CONNECTORS TO ANY OTHER CABLING THAN THOSE SPECIFIED BY HDL THERAPEUTICS.

- THE HDL THERAPEUTICS PDS-2 DELIPIDATION SYSTEM DOES NOT DETECT DISCONNECTION OF SPIKES OR LUERS IN THE TUBING SET BEFORE, DURING OR AFTER THE DELIPIDATION PROCESS. THE OPERATOR SHALL MONITOR ALL TUBING CONNECTIONS DURING PROCESSING.
- DO NOT UNLOAD DISPOSABLES UNTIL THE PDS-2 HAS INDICATED THAT PROCESSING HAS BEEN COMPLETED.
- DO NOT PLACE ANY OPEN FLUID CONTAINERS ON OR NEAR THE DEVICE SYSTEM.
- ALWAYS SHUT DOWN THE SYSTEM COMPLETELY AFTER COMPLETING A DELIPIDATION PROCESS. DO NOT START ANOTHER DELIPIDATION PROCESS WITHOUT FIRST SHUTTING THE SYSTEM DOWN.
- BEFORE EACH USE OF THE HDL THERAPEUTICS PDS-2 DELIPIDATION SYSTEM, INSPECT ALL TUBING TO ENSURE THEY ARE NOT KINKED OR TWISTED. TUBING THAT IS OCCLUDED, OR PARTIALLY OCCLUDED, MAY LEAD TO THE PROCEDURE NOT OPERATING CORRECTLY.
- NO PARTS SHOULD BE REPAIRED OR REPLACED EXCEPT BY A QUALIFIED HDL THERAPEUTICS SERVICE REPRESENTATIVE.
- ASSEMBLY, ADJUSTMENTS, ALTERATIONS, OR REPAIRS SHOULD ONLY BE CARRIED OUT BY PERSONS AUTHORIZED BY HDL THERAPEUTICS.
- THE SYSTEM SHOULD BE TURNED OFF PRIOR TO CLEANING TO AVOID ELECTRICAL SHOCK OR DAMAGE TO THE SYSTEM.
- THE SYSTEM SHOULD BE UNPLUGGED PRIOR TO SERVICING.
- SERVICING SHOULD ONLY BE PERFORMED BY QUALIFIED PERSONNEL FROM HDL THERAPEUTICS.
- PROPER PRECAUTIONS MUST BE TAKEN FOR CLEANING POTENTIALLY INFECTIOUS MATERIALS OFF OF THE DEVICE.
- ALL ELECTRICAL INSTALLATIONS MUST COMPLY WITH LOCAL ELECTRICAL CODES AND HDL THERAPEUTICS REQUIREMENTS.
- ANY EQUIPMENT CONNECTED TO ANALOG OR DIGITAL INTERFACES MUST COMPLY WITH IEC STANDARDS, WHERE APPLICABLE.
- SYSTEM CONFIGURATIONS MUST COMPLY WITH IEC 60601-1 STANDARD AND BE VERIFIED BY APPROPRIATELY TRAINED PERSONNEL. COMPLIANCE WITH ALL RELEVANT INTERNATIONAL STANDARDS

ELECTROMAGNETIC EMISSIONS AND COMPATIBILITY) MUST BE ENSURED.”

- REPORT IMMEDIATELY TO THE RESPONSIBLE SERVICE PERSONNEL ANY OF THE FOLLOWING CONDITIONS. DO NOT USE THE HDL THERAPEUTICS PDS-2 DELIPIDATION SYSTEM UNTIL CORRECTIVE ACTION HAS BEEN TAKEN.
 - Damaged or worn power cord, plug, or receptacle
 - Switches that are loose or do not operate with a positive action
 - A system that has been subject to physical shock or liquid spills on the electronics
 - A system that has given anyone an electrical shock while in use
 - A system that appears to be overheating.
- DO NOT RUN THE PDS-2 WITHOUT DISPOSABLES AS SPECIFIED BY AND INSTALLED ACCORDING TO THESE OPERATING MANUAL INSTRUCTIONS.
- KEEP HAIR AND CLOTHING AWAY FROM PUMP ROLLERS AND ANY OPEN ROTATING PUMP SLOTS TO AVOID THE POSSIBILITY OF HAIR OR CLOTHING BEING CAUGHT.
- EACH OPERATOR SHOULD BE THOROUGHLY FAMILIAR WITH THE HDL THERAPEUTICS PDS-2 OPERATOR'S MANUAL. ALL PROCEDURES SHOULD BE PERFORMED BY QUALIFIED AND TRAINED PERSONNEL.
- DISPOSABLE PRODUCTS MAY BE SUBJECT TO OCCASIONAL FAILURE WHICH COULD RESULT IN THE LOSS OF PLASMA, OR INTRODUCTION OF AIR OR CONTAMINATION INTO THE TUBING SET. IT IS VERY IMPORTANT THAT THE OPERATOR CAREFULLY OBSERVE FOR LEAKS DURING PRIMING AND USE OF THE DISPOSABLE TUBING SET.
- USE ASEPTIC TECHNIQUE THROUGHOUT ALL PROCEDURES.
- BE CAREFUL NOT TO STRETCH OR KINK THE TUBES WHEN INSTALLING THE DISPOSABLE TUBING SET ONTO THE VALVES OR PUMP.
- ENSURE THAT TUBING LINES ARE ATTACHED TO CORRECT FLUIDS AND BAGS DURING LOADING.
- VISUALLY VERIFY THAT FLUID IS FLOWING INTO THE LINES AND BAGS AS SPECIFIED IN THIS HDL THERAPEUTICS PDS-2 OPERATORS MANUAL.

- PUMP AND MIXING PLATFORM RATES ARE CONTROLLED AUTOMATICALLY WHEN THE HDL THERAPEUTICS PDS-2 DELIPIDATION SYSTEM IS OPERATING. DO NOT ATTEMPT TO IMPEDE THEIR OPERATION.
- INSTALL ALL BAGS FIRMLY ONTO THEIR INSTALLATION POSTS. THIS WILL ENSURE PROPER OPERATION AND FLUID FLOW, AND PREVENT BAGS OR LINES FROM TOUCHING THE FLOOR DURING INSTALLATION AND PROCESSING.
- IT IS THE RESPONSIBILITY OF THE HEALTH CARE INSTITUTION TO ADEQUATELY PREPARE AND IDENTIFY THE PLASMA FOR RETURN TO PATIENT.
- BE SURE ALL LUER AND SPIKE CONNECTIONS ARE SECURE.
- PROPERLY DISPOSE OF ALL BIOHAZARD AND/OR CHEMICAL WASTE.
- WHEN TRANSPORTING THE PDS-2, ENSURE THAT NO DISPOSABLES ARE PRESENT ON THE INSTRUMENT (TUBING, BAGS, LIQUIDS).
- EXERCISE CAUTION WHEN TRANSPORTING THE PDS-2 ACROSS THRESHOLDS IN ORDER TO PREVENT POSSIBLE TIPPING.
- DO NOT POSITION THE PDS-2 TOO CLOSE TO A WALL OR OTHER OBSTRUCTION SUCH THAT IT WOULD BE DIFFICULT TO DISCONNECT THE SYSTEM FROM THE AC POWER SUPPLY.
- DO NOT PLUG ANY ADDITIONAL ELECTRICAL CONNECTORS OR APPLIANCES INTO THE UNINTERRUPTED POWER SOURCE (UPS).
- DO NOT REUSE SOLVENT.
- DO NOT REUSE CHARCOAL COLUMN.
- CAUTION: MEDICAL ELECTRICAL EQUIPMENT NEEDS SPECIAL PRECAUTIONS REGARDING EMC AND NEEDS TO BE INSTALLED AND PUT INTO SERVICE ACCORDING TO THE EMC INFORMATION PROVIDED IN SECTION 22 THIS DOCUMENT.
- CAUTION: PORTABLE AND MOBILE RF COMMUNICATIONS EQUIPMENT CAN AFFECT MEDICAL ELECTRICAL EQUIPMENT.

APPROPRIATE CAUTIONS SHOULD BE EMPLOYED.

5. Potential Risks

Below is a list of the potential adverse effects (i.e., complications) associated with either the plasmapheresis procedure or the use of the device:

- Risks of any procedure involving extracorporeal circulation, including:
 - Abdominal discomfort
 - Anemia
 - Angina/chest pain
 - Arrhythmia
 - Blood loss
 - Bradycardia
 - Chills
 - Diaphoresis
 - Dyspnea
 - Fainting
 - Flushing/blotching
 - Headache
 - Hemolysis
 - Hyperventilation
 - Hypotension
 - Itching/hives
 - Lightheadedness
 - Nausea /vomiting
 - Pallor
 - Paresthesia due to citrate infusion
 - Shortness of breath
 - Tachycardia
 - Vasovagal reaction
- Vascular access problems, including:
 - Air embolism
 - Blood clotting
 - Excessive bleeding from the anticoagulant
 - Hematoma formation at the site of venipuncture
- Anemia
- Asthenia
- Coagulopathy
- Cyanosis
- Dizziness

- Fatigue
- Fever
- Fluid imbalance
- Generalized weakness
- Heart block
- Hyperkalemia
- Hypersensitivity reactions
- Infusion site pain
- Metal taste in mouth
- QT Interval abnormality
- Significant blood or plasma loss from extracorporeal circuit leaks
- Sweating
- If serum albumin is administered:
 - Allergic reaction
 - Transmission of infectious diseases

6. Clinical Experience

The clinical study, HDL Acute Lipid Optimization in Homozygous Familial Hypercholesterolemia (HALO-FH), evaluated the safety and effectiveness of the PDS-2 System. Six (6) subjects with Homozygous Familial Hypercholesterolemia (HoFH) were enrolled in the clinical study. These subjects were scheduled for 7 delipidation treatment sessions (i.e., serial infusions of autologous selectively delipidated HDL/pre β enriched plasma following use of the PDS-2), with 1 infusion per week. Treatment sessions lasted approximately 7-9 hours each and included the following activities: assessment/pre-plasmapheresis, plasmapheresis, PDS-2 System Processing; reinfusion, and observation. Follow-up was conducted at 2 weeks, as well as 3, 6, 9, and 12 months after the last infusion.

Overall, the 6 HoFH subjects who presented with at least one coronary plaque and their plasma was selectively delipidated with the HDL Therapeutics' PDS-2 System were imaged successfully before and after the therapy with complete data provided. Among the six patients, 16 plaques were identified at baseline and follow-up and no new plaques were detected in follow-up.

The pre-specified primary endpoints for the HALO-FH study were: (1) the change in coronary atheroma area as assessed by coronary CT angiography following treatment and (2) cumulative adverse events, serious adverse events, and unanticipated adverse device events. The pre-specified secondary endpoint for this study was the change in total atheroma volume as assessed by coronary CT angiography following treatment. These results were analyzed on a per-plaque level and the PDS-2 therapy was shown to reduce the plaque volume and area.

As described in detail in **Table 1** below, there was a statistically significant 18% reduction (P=0.023) in the total atheroma cross-sectional area between baseline and follow-up, which was the primary endpoint of the study. Additional exploratory analyses measured the plaque composition and volume. These results showed that the reduction in total atheroma cross-sectional area was driven by a reduction of low-density (-38%) and necrotic core (-33%) portions of the plaque, known to be found in high- risk plaques prone to rupture and are associated with increased rate of acute coronary syndrome. Similarly, evaluation of the secondary endpoint demonstrated that the volume of low density (-42%) and necrotic core portions (-35%) of the plaque were found to be reduced.

Table 1 - Summary Statistics and Testing Differences Per-Plaque

N=16 plaques mean ± SD	Baseline	Follow-up	Absolute Change ^a	Relative change	P-value ^b
Atheroma cross-sectional area ^c -mm²					
Total	9.9 ± 3.5	8.2 ± 2.4	-1.8 ± 2.8	-18%	0.023 ^d
Non-calcified	9.0 ± 3.5	7.2 ± 1.9	-1.8 ± 2.5	-20%	
Calcified	0.9 ± 0.9	1.0 ± 1.1	+0.1 ± 0.6	+11%	
NCP					
Low-density NCP	1.6 ± 0.8	1.0 ± 0.5	-0.6 ± 0.6	-38%	
Necrotic core	1.5 ± 0.7	1.0 ± 0.5	-0.5 ± 0.6	-33%	
Fibrofatty	4.0 ± 1.9	3.2 ± 0.8	-0.8 ± 1.7	-20%	

^a Difference = Follow-up — Baseline; ^b Wilcoxon signed rank test (STATA 15.0); ^c Area = plaque volume / plaque length; ^d The plaques were treated as independent observations.

Additional evaluation of the change in total atheroma cross-sectional area and volume on a per-patient level showed that a majority of these HoFH patients received a benefit from PDS-2 treatment. During the study period, 11/16 (69%) plaques regressed with respect to total area (i.e., reduction in total plaque area). When focusing on the highest risk low-density portions of the plaque and necrotic core portions of the plaques, overall, 14/16 (88%) experienced regression of these key components of the plaque. On a per-patient basis, in 4/6 (67%) patients, all plaques demonstrated regression of the low-density area and necrotic core. In one subject, 4/5 plaques experienced regression, while in the last subject, their single plaque did not regress.

Table 2 summarizes the type and number of adverse events (AEs) observed during the HoFH study. Overall, 30 AEs were reported for 5 subjects. Of the 30 reported events, 29 were classified as mild (96.7%) and 1 was classified as moderate (insomnia) (3.3%). None of the AEs were classified as severe. Only one

(asthenia post-treatment) was considered to be potentially (possibly) related to the device.

Table 2 - Adverse Event Summary for HoFH Subjects (n=6)

Type of Adverse Event	Number of Events
Metal taste in mouth	7
Asthenia post treatment	5
Headache	2
Generalized weakness	2
Vasovagal syncope	2
Infusion site pain	2
Hot flush	1
Insomnia	1
Pain related to arm surgery	1
Occasional nocturne dry cough	1
Cough with secretion	1
Pain in inferior limbs	1
High blood pressure	1
Neck pain	1
Lightheadedness	1
12 hr. post treatment fatigue	1

Patient vital signs were also measured during the HoFH study, including heart rate, respiratory rate, blood pressure, and body temperature. Clinical hypotension (systolic blood pressure < 90 mmHg or diastolic blood pressure < 60 mmHg) was observed during 32 (71.1%) of the 45 infusion visits. Clinical bradycardia (heart rate < 60 bpm) was observed during 27 (60.0%) of the 45 infusion visits and clinical tachycardia (resting heart rate > 100 bpm) was observed on 1 (2.2%) of the 45 infusion visits. Hypotension, bradycardia, and tachycardia were not considered to be adverse events if no physical symptoms were present. Additionally, no febrile episodes (body temperature $\geq 38^{\circ}\text{C}$ and at least 1°C increase in body temperature from baseline) were observed. A summary of these vital sign fluctuations are shown in **Table 3** below.

Table 3 - Vital Sign Summary for HoFH Subjects (n=6)

Vital Sign Monitoring	Number of Episodes
Hypotensive Episodes	32
Bradycardia	27
Tachycardia	1
Febrile Episodes	0

Finally, HoFH patients were followed every 3 months for up to 12 months after their last treatment. A summary of the follow up AEs is provided in **Table 4**. The majority of AEs observed were of mild severity and most have resolved. None of the events were considered related to either the device or the clinical procedure.

**Table 4 – HALO-FH Study Adverse Event Follow-up Data (3, 6, 9, and 12 mo.)
(n = 4)***

Type of Adverse Event	Number of Events
Bronchitis	2
Light Sleep Apnea	1
Upper Tract Respiratory Infection	1
Anemia	1
Right Thumb Skin Mycosis	1
Feeling of Pressure Both Eyes	1
Increased Insomnia	1
Nose Squamous Cell Carcinoma in situ	1
Type 2 Diabetes	1
Back Pain	1
Neck Pain	1
Right Knee Pain	1
Enteritis	1
Arthritis L5-S1	1
Dorsal Spondylosis	1
Influenza	1
Thickening Left Achilles Tendon Xanthoma	1
Increased Headache Frequency	1
New Onset Exertional Chest Pain	1

* Complete AE follow-up data is only available for 4 of the 6 enrolled patients as 2 patients withdrew from the study prior to completion of 12-month follow-up visits. One patient withdrew consent after the 6-month follow-up time point. This patient did not report any AEs prior to study withdrawal. The second patient only participated in the 2-week follow up visit and did not report any AEs at that time. This patient did not wish to participate in any of the 3, 6, 9 and 12-month follow up visits and subsequently withdrew consent.

Patient vital signs, including systolic blood pressure, diastolic blood pressure, heart rate, and temperature were measured at the 3, 6, 9, and 12 month follow-up visits. There were no unexpected or concerning vital sign measurements observed during the follow-up period and all measurements were determined to be clinically insignificant.

In addition to the six subjects with HoFH that were studied, a second trial used the PDS-2 System to evaluate 14 patients diagnosed with acute coronary syndrome (ACS). While this is a different patient population, the clinical data from this ACS study provided supportive information related to device safety.

During the ACS study, 2 serious adverse events (SAEs) were reported for patients in the treatment group and 2 SAEs were reported for patients in the placebo group, all of which were hospitalizations surrounding angiography or coronary

revascularization, which were anticipated events.

AEs were reported in 7 of the 14 patients treated with the PDS-2 System. Most AEs reported were of mild severity and were resolved. **Table 5** summarizes the type number, and relatedness of the AEs observed in the treatment group during the ACS study.

Table 5 - Adverse Event Summary for ACS Subjects in the PDS-2 Group (n=14)

Type of Adverse Event	Number of Events	Related to Plasma Collection	Related to Reinfusion	Related to Device*
Hypotension	5	Probable	Not Related	Not Related
Heart block	3	3 Not Related	1 Not Related 2 Remotely Possible	Not Related
Bradycardia	1	Probable	Not Related	Not Related
Hyperkalemia	2	Possible	Possible	Not Related
Revascularization, Percutaneous Coronary Intervention with drug eluting stent (Non Target Vessel)	1	Not Related	Not Related	Not Related
Other	2	Not Related	Not Related	Not Related
Cyanosis	1	Probable	Not Related	Not Related
Pallor	1	Probable	Not Related	Not Related
Peptic Ulcer	1	Not Related	Not Related	Not Related
Sweating	1	Probable	Not Related	Not Related

**AEs not related to the device were classified as "Anticipated" or "Subject/Non-Device Related" in the clinical study report.*

Acceptable residual levels of the delipidation solvent mixture in the plasma output were set as follows: Sevoflurane \leq 35.0 ppm; n-Butanol \leq 20.0 ppm. Plasma from the ACS trial tested directly by Gas Chromatography on 98 bags of patient's treated plasma yielded the following results:

Sevoflurane - 97 *below* limit-of-detection, 1 @ 3.4 ppm;
n-Butanol – 98 *below* limit-of-detection

7. Introduction

7.1 Theory of Operation

The HDL Therapeutics PDS-2 System is intended to reduce coronary atheroma in adult patients with homozygous familial hypercholesterolemia (HoFH) who are either inadequately responsive or intolerant of maximal therapy for HoFH.

The PDS-2 System is a therapeutic medical device composed of an automated processor (hardware), sterile single use disposables supplied as a PDS-2 kit, and organic solvents sevoflurane and n-butanol. The device treats autologous plasma collected from a subject via an approved plasmapheresis device using citrate as an anticoagulant. The plasma from the patient is collected into a sterile bag via standard apheresis techniques. The plasma is then brought over to the PDS-2 device for processing. It is important to note that the PDS-2 device is not connected to the patient at any time. The patient's plasma is treated offline by the System, pumped into an integral sterile bag, brought back to the patient's location, and then reinfused back into the patient via a separate standard infusion pump after processing.

The PDS-2 was designed in consideration of a scientific article regarding the proposed mechanisms by which cholesterol can be removed from cells (Brewer, B.J. Clin. Endocrinol. Metab, May 2011, 96(5):1246-1257). In this article, the receptor ABCA1 was identified as a "gate" for allowing cholesterol to be released by cells. It was suggested that pre β -HDL is the only form of HDL that can bind to the ABCA1 receptor, and the other form of HDL (α -HDL) cannot bind to this receptor. Thus, it is hypothesized that circulating pre β -HDL particles attach to the ABCA1 receptor site to enable reduction of cholesterol-laden plaques. The PDS-2 System is designed with the intent to target this hypothesized mechanism, to potentially increase the availability of pre β -HDL particles to enhance the body's delipidation capability and thereby reduce cholesterol-laden plaques. However, this proposed mechanism of action for this device has not been definitively proven in any non-clinical or clinical studies.

7.2 System Operation

The HDL Therapeutics PDS-2 System is to be operated only by HDL Therapeutics trained and certified Delipidation technicians. The system is not intended to be operated by personnel at the clinical site.

7.3 System Contents/Components

- PDS-2 CONSOLE
- PDS-2 INSTRUMENT

- CONNECTORS/CABLES

120VAC System

DESCRIPTION	LENGTH (M)	SHIELDING	FERRITES
AC Mains Cable – permanently connected to UPS	2	NO	YES
Power Cable for Computer	2	NO	NO
Power Cable for Monitor	1.8	NO	NO
VGA Cable for Monitor	1.5	YES	YES
USB A-A Cable	2	YES	NO
RS-232 Extension Cable	0.3	YES	NO
USB to RS-232 Converter Cable	1.8	YES	NO

230VAC System

DESCRIPTION	LENGTH (M)	SHIELDING	FERRITES
AC Mains Cable	2	NO	YES
Power Cable for Computer	1	NO	NO
Power Cable for Monitor	1	NO	NO
VGA Cable for Monitor	1.5	YES	YES
USB A-A Cable	2	YES	NO
RS-232 Extension Cable	0.3	YES	NO
USB to RS-232 Converter Cable	1.8	YES	NO

- DISPOSABLES

- PLASMA DELIPIDATION SET H3008102
- SOLVENT-IN BAG H3008614
- SOLVENT TRANSFER SET H3008201

The Disposables are sterilized by gamma irradiation, and are for single use only; do not attempt to clean or re-sterilize any Disposables. Examine the packaging to verify that seals are intact; if not, it must be assumed that the device is not sterile and must not be used.

Do not use beyond the expiration date marked on outer package.

- Charcoal Column Gambro P/N 300 C
- SOLVENTS. DESCRIPTIONS AND PART NUMBERS.
 - SEE APPENDIX 1

7.4 System Layout

The system consists of three parts: the console which serves as the operator interface, the instrument which houses the sensors, actuators, and the disposable tubing set which installs onto the instrument and carries the fluids through the delipidation process. Figure 1 on the next page shows the locations of the components and the designations used in this manual. “V” refers to a valve and “LC” refers to a load cell.

The system is to be placed in such a manner that the power cord from the Uninterruptable Power Supply (UPS) can be accessed by the operator at all times in case service needs to be removed from the system quickly.

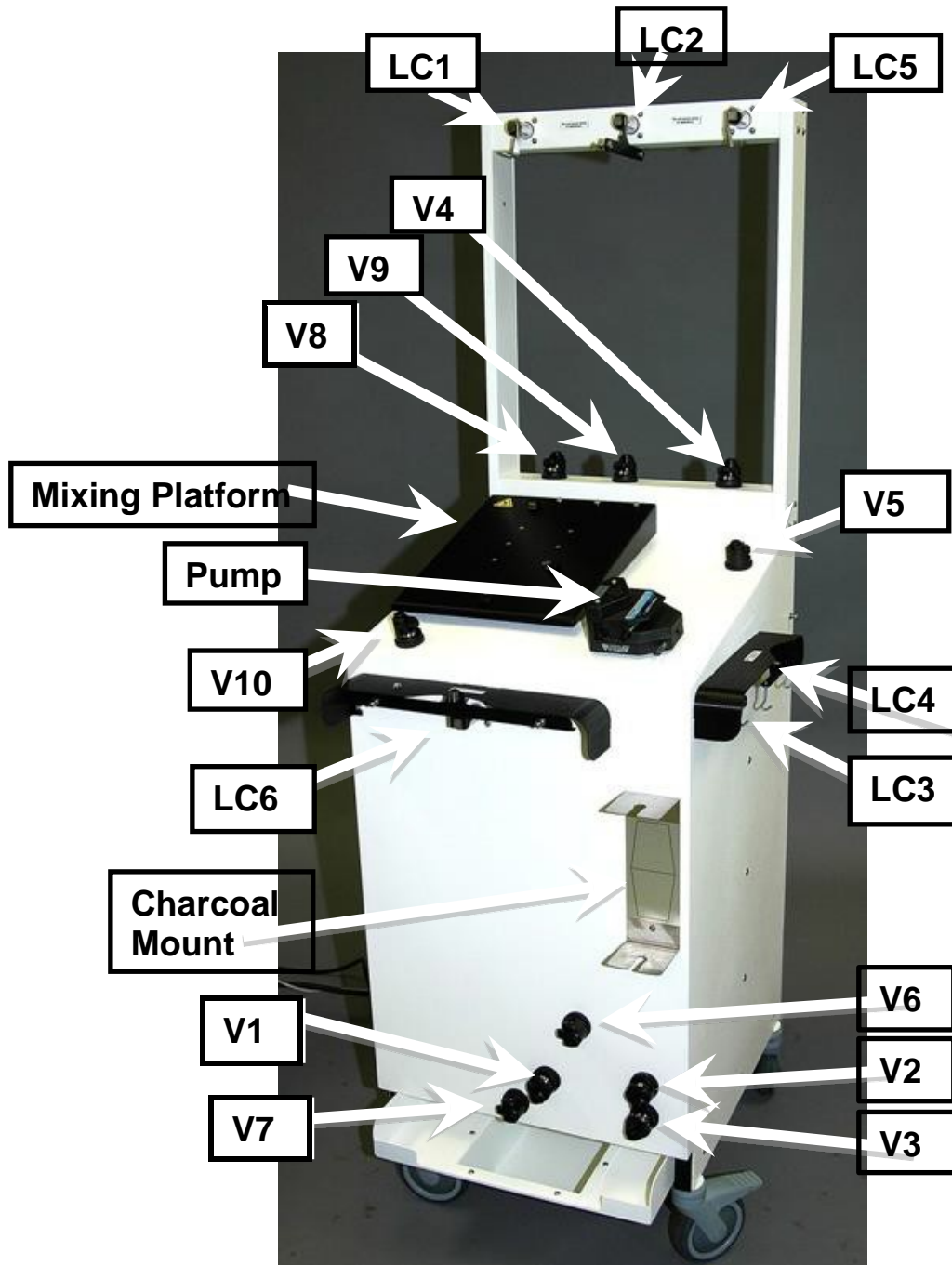


Figure 1: Locations of Major Components on Device

The schematic diagram in Figure 2 below shows the major components of the device with respect to their location in the fluid path.

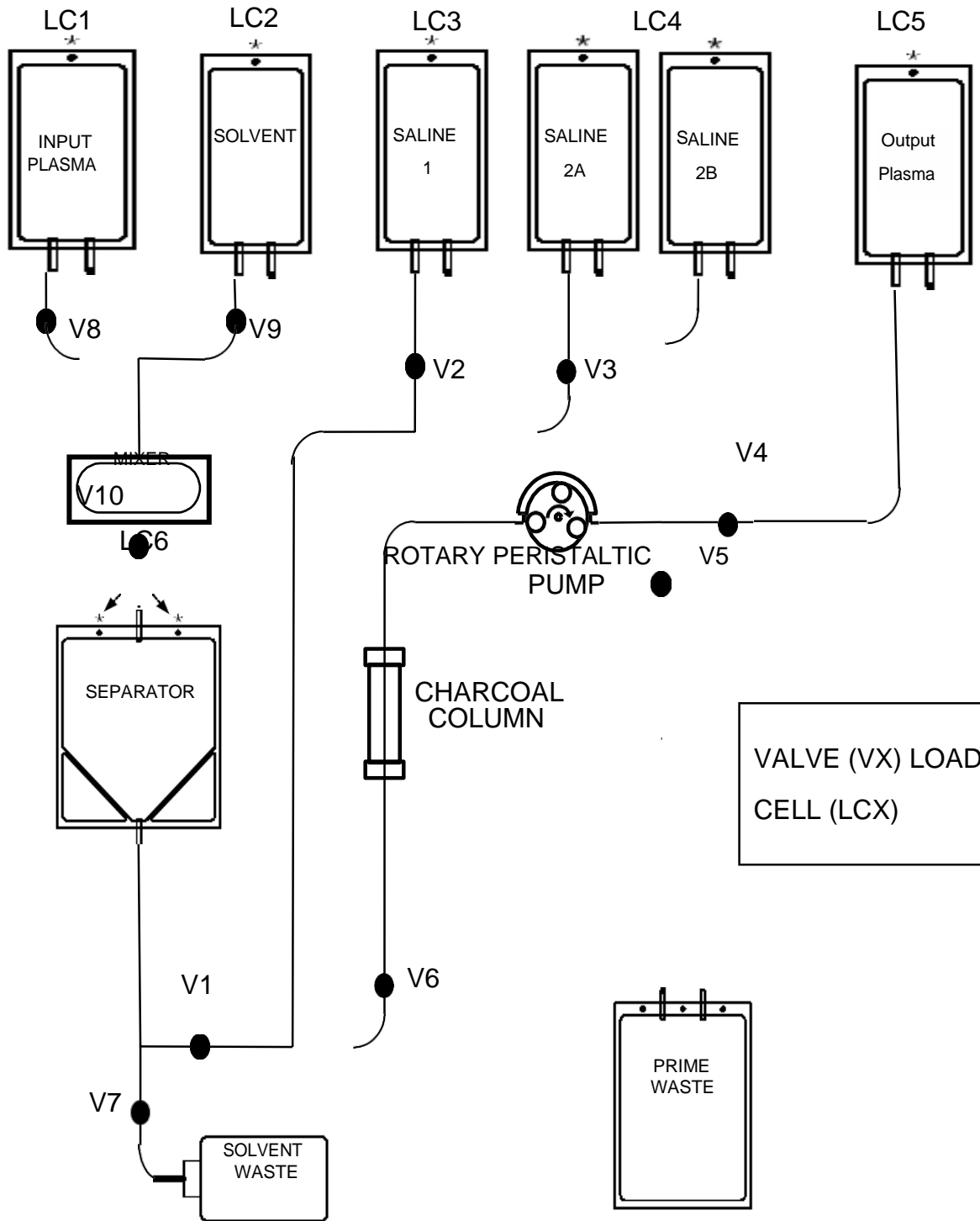


Figure 2: System Schematic Diagram

7.5 The Delipidation Process Step by Step

Diagrams shown below describe the steps of the delipidation process in the order in which they are performed.

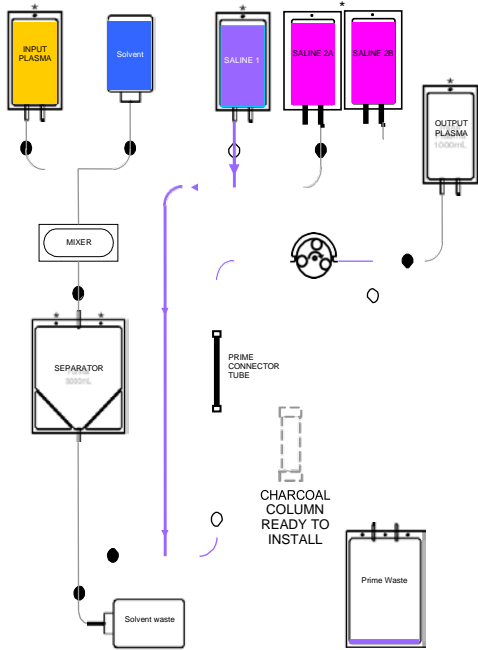
Solvent preparation is described in **APPENDIX 1** of this User manual/Instructions for Use.

<p style="text-align: center;">WARNING</p> <p style="text-align: center;">SOLVENT PREPARATION SHOULD ONLY BE COMPLETED BY TRAINED AND CERTIFIED OPERATORS.</p>

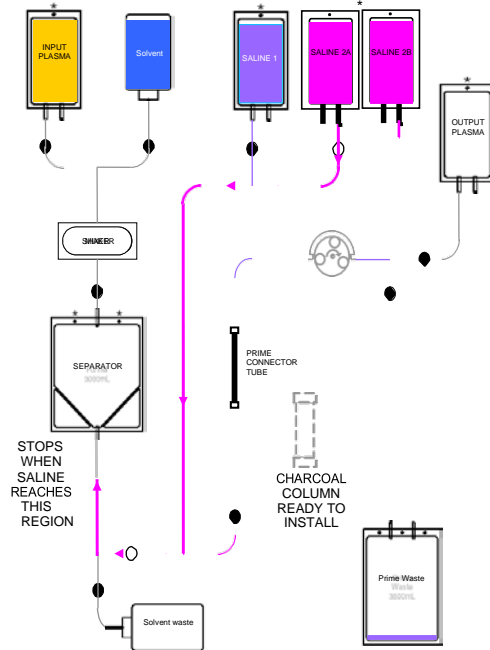
Plasma and solvent are introduced into a specially designed mixing bag in precise quantities and volumetric ratios. The solvent and plasma are then mixed in an orbital fashion for a prescribed period. Delipidation occurs during this step. The mixture is then drained into a separator bag. Each batch is mixed and drained into the separator bag until the input plasma is fully processed. When the separator bag reaches capacity, excess solvent is drained to the solvent waste bag.

The timed suspension in the separator bag separates the plasma and solvent again into distinct parts so the solvent can be drained into the solvent waste bag. Some solvent, however, remains dissolved in the plasma. This residual solvent is substantially removed by passing the plasma through a specially-designed column. The output plasma contains delipidated HDL.

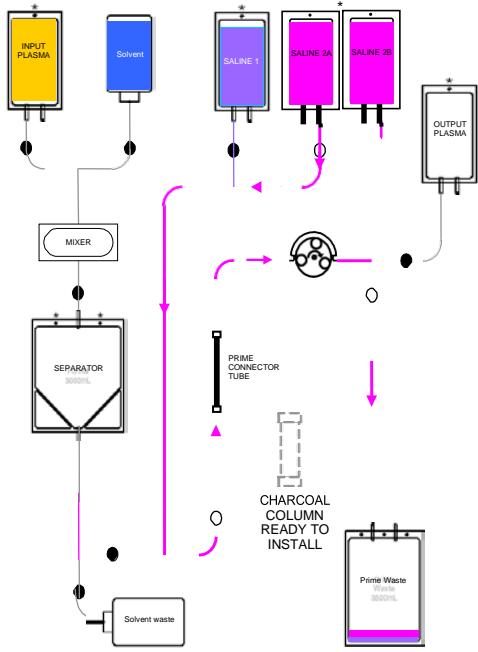
Delipidation Steps 1-4



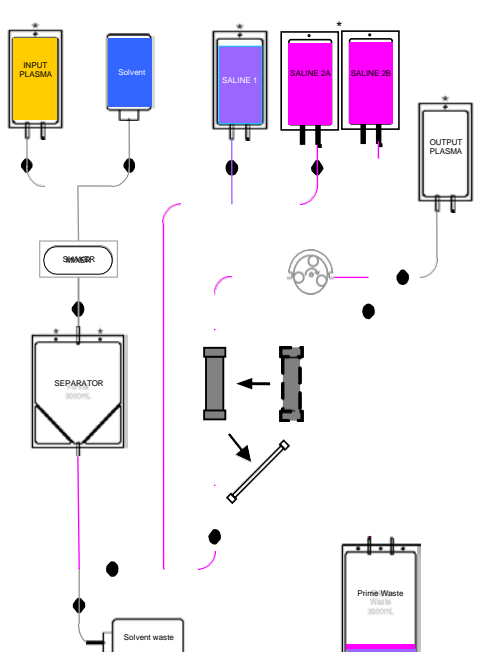
Step 1, Saline Pre-Prime 1



Step 2, Separator Pre-Prime

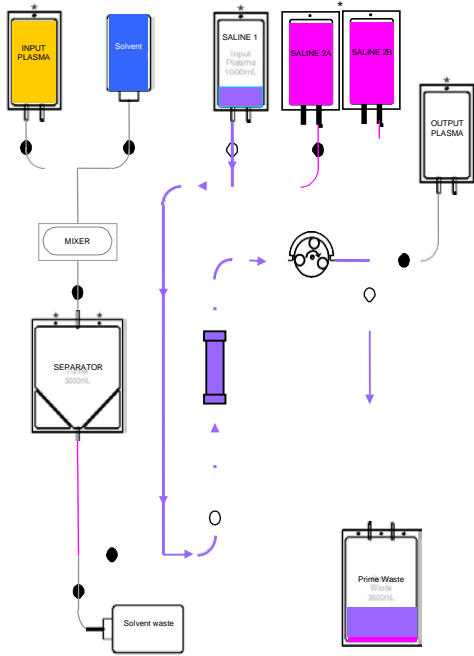


Step 3, Saline Pre-Prime 2

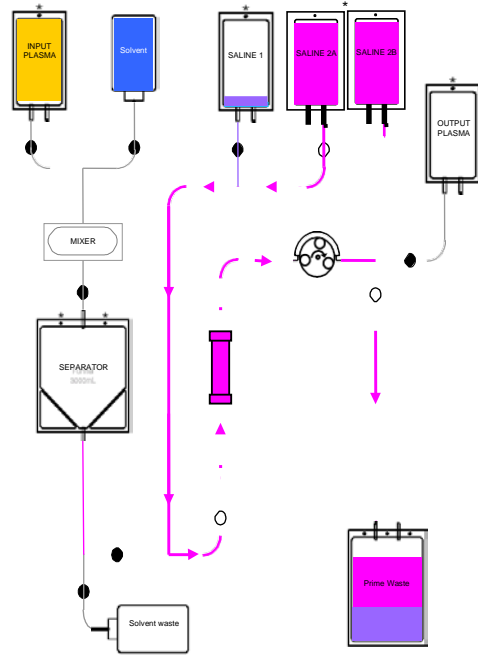


Step 4, Install column

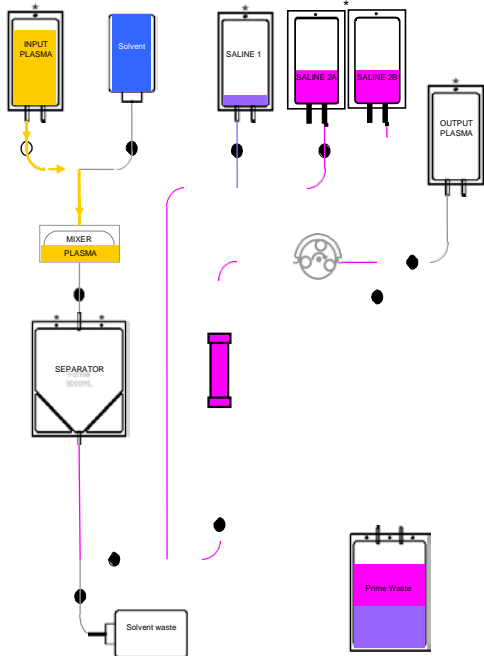
Delipidation Steps 5-8



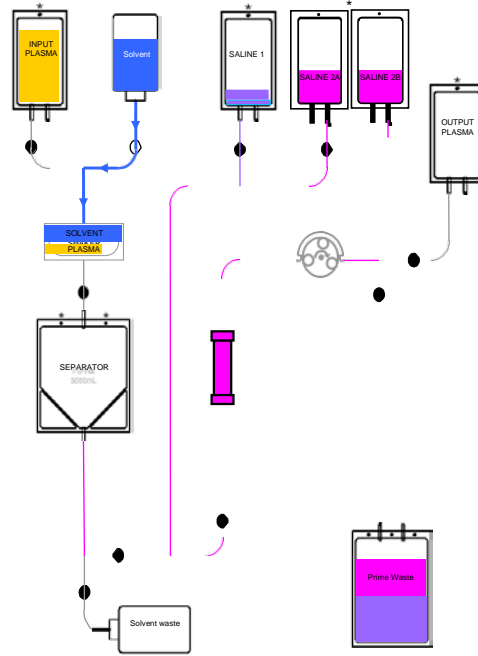
Step 5, Saline Prime 1



Step 6, Saline Prime 2

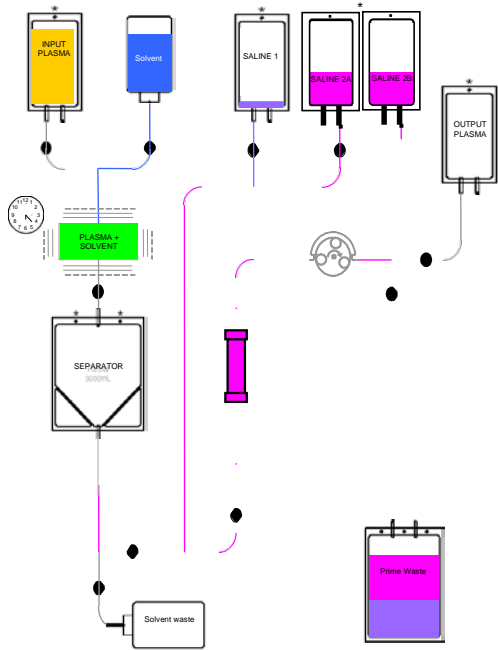


Step 7, Plasma Introduction

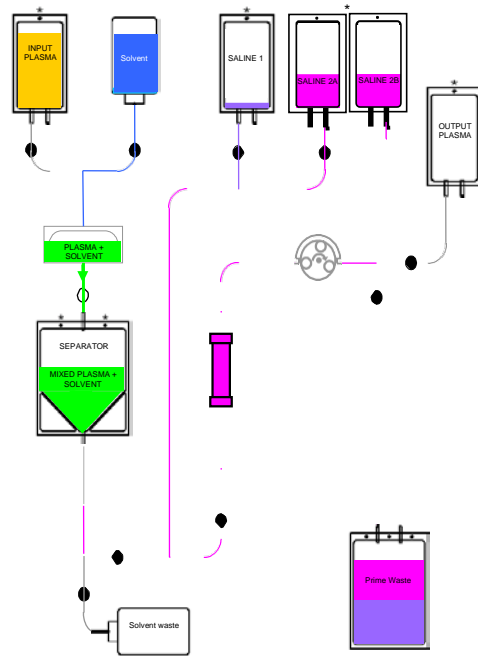


Step 8, Solvent Introduction

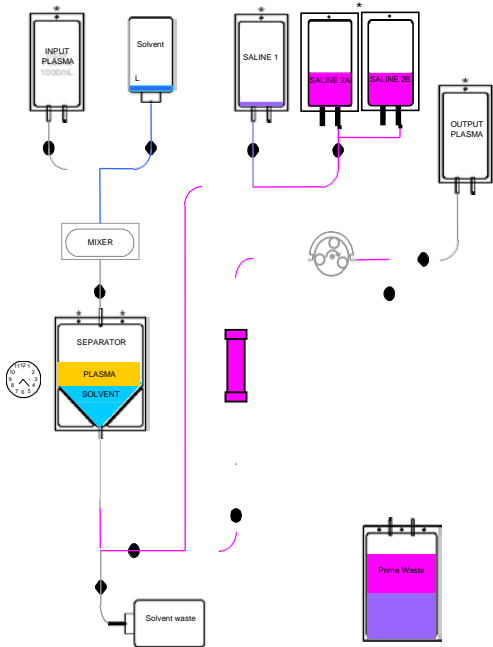
Delipidation Steps 9-12



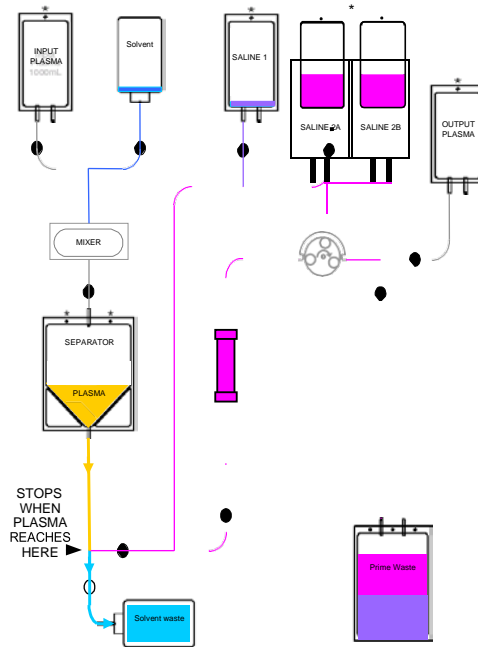
Step 9, Mixing



Step 10, Transfer To Separator

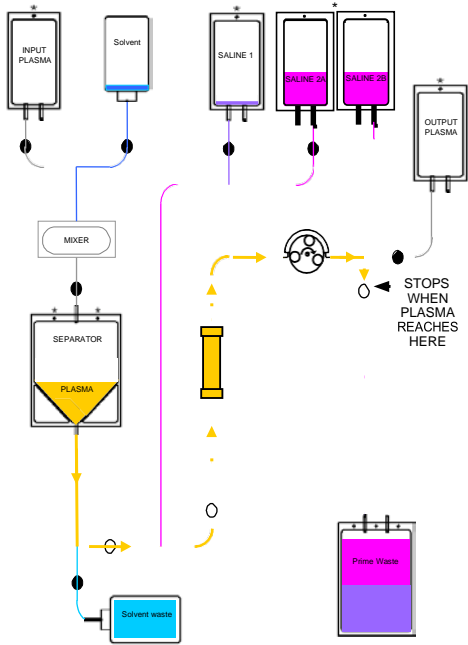


Step 11, Separation

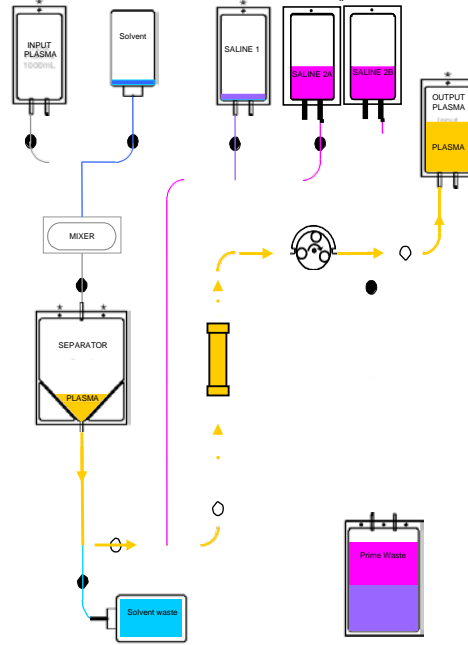


Step 12, Bulk Solvent Removal

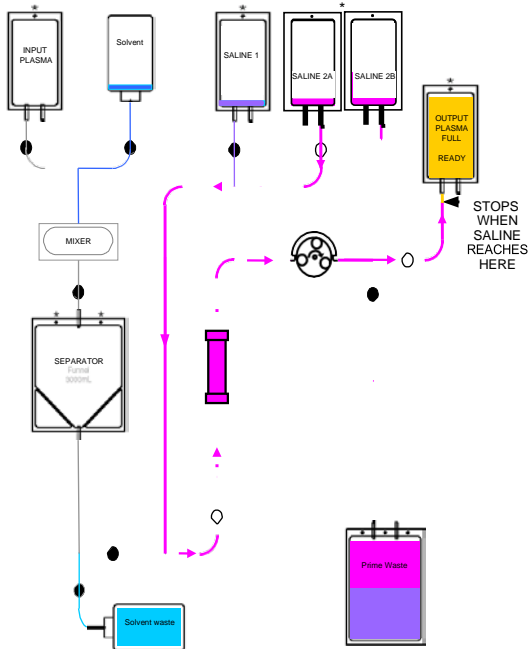
Delipidation Steps 13-15



Step 13, Saline Purge and start of solvent removal



Step 14, Residual Solvent Removal



Step 15, Saline Chase

8. System Set Up

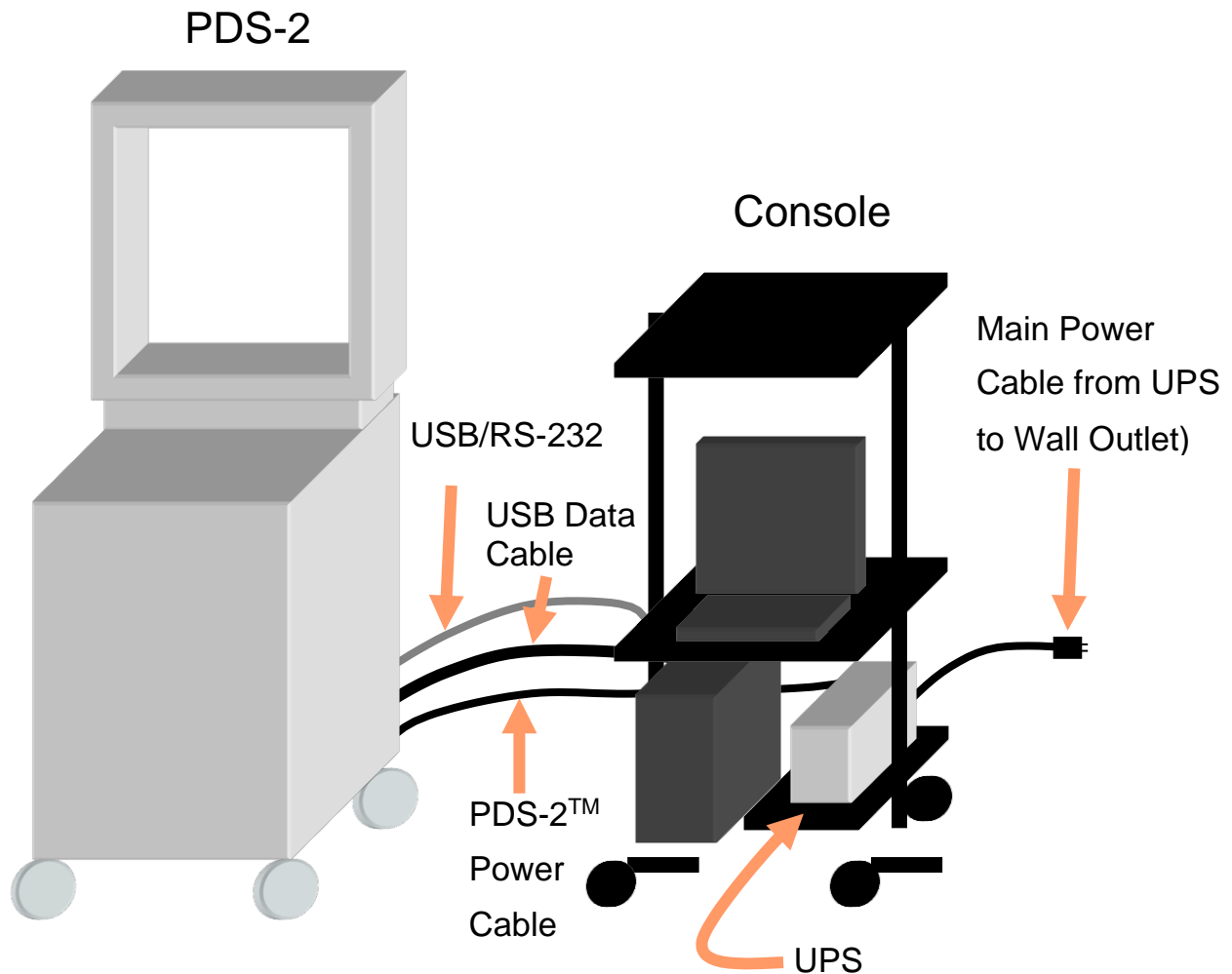


Figure 3: System setup showing PDS-2 and console with cables.

8.1 Instrument

The instrument carries the disposable tubing set and is responsible for transporting the plasma, solvent, and priming solutions to accomplish delipidation.

Position the instrument in a convenient location.

Lock all four casters.

Inspect the instrument for obvious defects or damage.

8.2 Console

The console is the computer system which controls the instrument and reports the progress of delipidation to the operator. The Uninterruptible Power Supply (UPS) shares the cart with the console and ensures that delipidation is not compromised by an AC power interruption.

Position the console in a convenient location near the instrument.

8.3 Cables and Connections

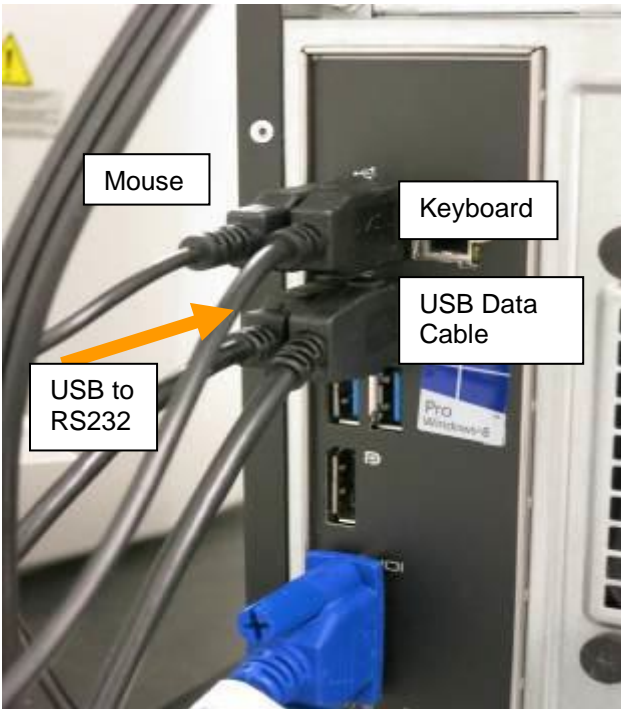
Connect the power cord of the instrument, the monitor, and the computer into the receptacles on the face of the UPS. Connect the power cord of the UPS into a grounded receptacle.

Connect the USB Data cable between the instrument and the computer.

The locations of the connectors are shown in Figure 4 a) and b). Tighten the screws of both plugs securely.

Connect the USB to RS-232 converter cable between the machine and the computer.

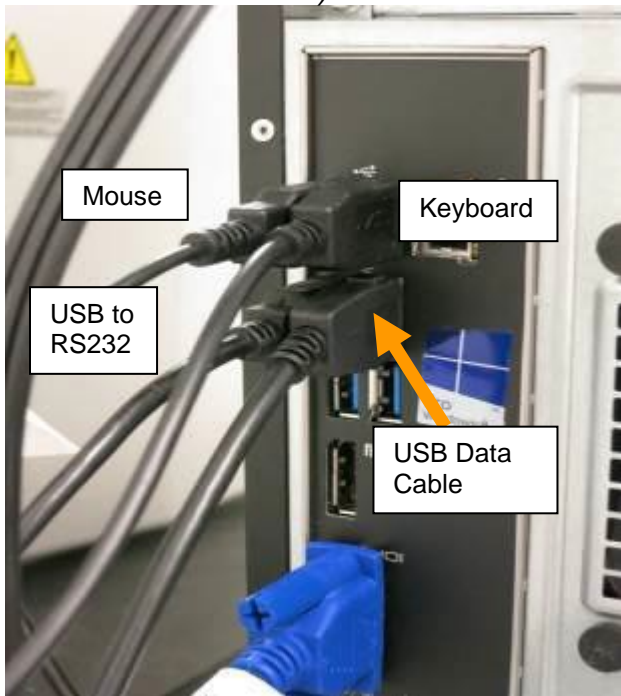
The locations of the connectors are shown in Figure 4 c) and d). Tighten the screws of plugs securely.



a)



b)



c)



d)

Figure 4 a-d: Cable Connections on the Instrument and console

8.4 Power On

Turn the UPS power on. The power switch is located on the front panel. It is best to allow 24-hour charging of the UPS before use if not previously charged.

Turn on the power of the computer and monitor.

Turn on the power of the instrument. The power switch is located on the left side near the bottom.

When prompted, enter the correct username and password, and click on “OK” when completed. The Main Menu will appear.

8.5 Main Menu



Figure 5: Main Menu

As shown in Figure 5, the Main Menu has two options: Delipidate, and Shutdown.

Selecting shutdown turns off the computer.

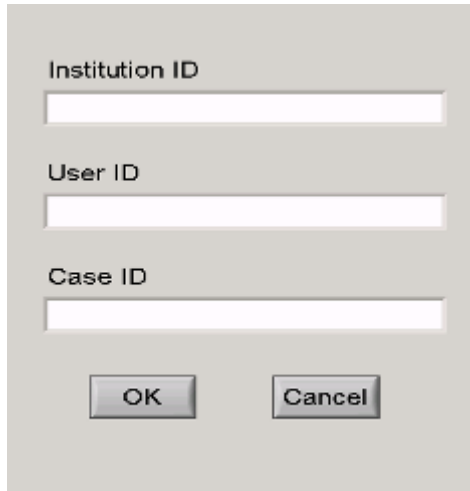
Selecting “Delipidate” begins the delipidation process.

8.6 Process Identification

Once “Delipidate” is selected from the Main Menu, the process identification dialog is displayed as shown in Figure 6.

Enter the Institution ID, Operator ID, and Case ID in the fields provided to help track delipidation records. Note that these fields are optional and may be left blank.

Press “OK” when process identification information has been entered. The Delipidation screen will appear.

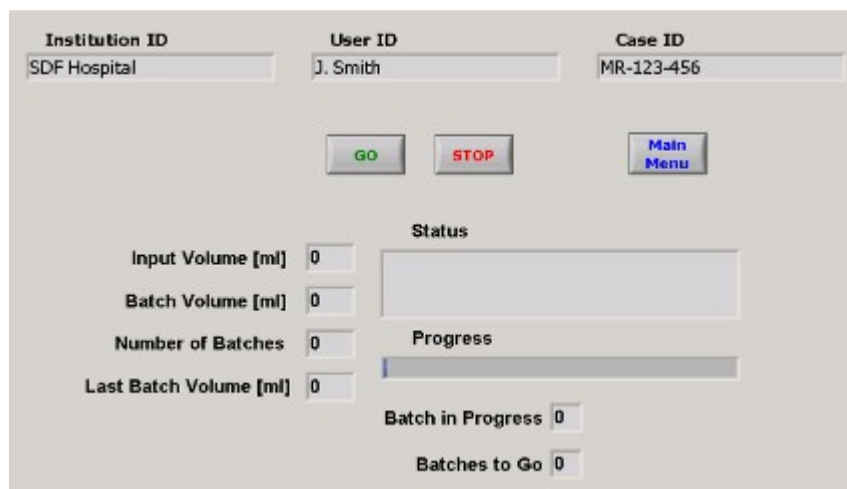


A dialog box for process identification. It contains three text input fields labeled "Institution ID", "User ID", and "Case ID". Below the fields are two buttons: "OK" and "Cancel".

Figure 6: Process Identification Dialog

8.7 Delipidation Screen

The delipidation screen allows the operator to start and stop the delipidation process, return to the main menu, and provides progress and status information while a delipidation is in progress.



The delipidation screen displays the following information and controls:

- Input fields for Institution ID (SDF Hospital), User ID (J. Smith), and Case ID (MR-123-456).
- Buttons for GO (green), STOP (red), and Main Menu (blue).
- Input fields for Input Volume [ml], Batch Volume [ml], Number of Batches, and Last Batch Volume [ml], all set to 0.
- Status and Progress sections with a text box for status and a progress bar.
- Batch in Progress and Batches to Go, both set to 0.

Figure 7 : Delipidation Screen

9. Collect Patient Plasma

A blood glucose test must be performed prior to plasma collection. The blood glucose test should make sure that the patient baseline glucose level is not <65 mg/dL.

Aseptically collect up to 1000 cc of autologous plasma into hospital-supplied plasma bag using standard plasmapheresis techniques, per the plasmapheresis system Instructions for Use and hospital standard processes for plasmapheresis using citrate as an anticoagulant. Delipidation process should be started within 1 hour of plasma collection. Plasma should be kept at room temperature.

10. Loading the Tubing Set

9.1 Opening the Container

Note: Observe the expiry dates on all sets, bags solutions, and column. Do not use expired materials.

Prior to opening any packaging, inspect for damage that may have compromised the sterility, discard any product where sterility may have been compromised.

Grasp the indicated corner of the Tyvek® lid and peel it back. Remove the tubing set and set the container aside. Inspect the tubing set for any damage that may have occurred during shipping.



Figure 8: Disposable tubing set with lid open

9.2 Installing the Set

Press “GO” on the delipidation screen. You will be prompted to load the disposable as shown in Figure 9. Press “OK”. All ten valves will open. Do not load the input plasma bag, solvent bag, or any priming solutions at this time.



Figure 9: Prompt to load disposable

The tubing set is in two pieces. There is one portion connecting the input plasma bag and solvent through to the charcoal column. The other portion connects the output of the charcoal column through the pump to the output plasma bag.

Check that all the Luer connections are tightened securely as shown in Figure 10.



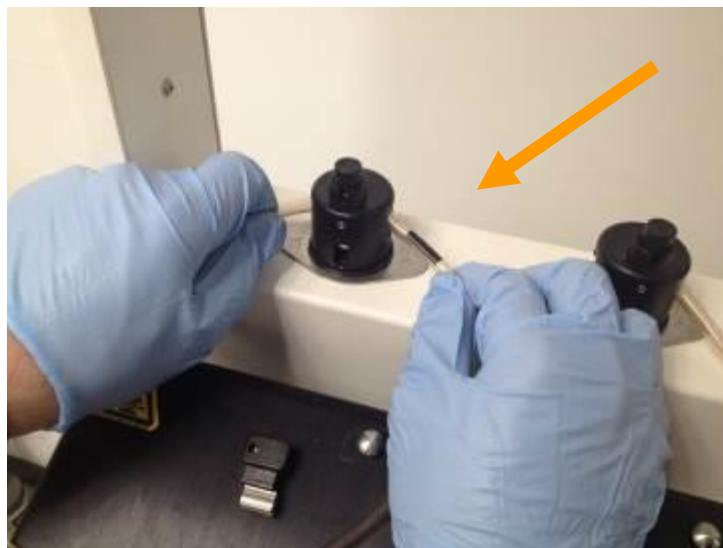
Figure 10: Checking Luer Connections

Note: Remember not to install any of the liquid-filled bags of plasma, solvent, or saline until prompted by the instrument.

Note: Observe all lines and bags during installation to avoid kinking or damage due to tearing, rupture, or puncture.

Perform the following steps to install the disposable (refer to Figure 1 for valve locations):

1. Insert the input plasma tubing into V8, aligning black mark on tubing to be on the right side of the pinch valve as shown.



2. Insert the solvent tubing into V9 (right of V8), aligning black mark of tubing to be on the left side of the pinch valve as shown.



3. Install the mixing bag on the mixing platform, mount the bag on the grommets, and the tubing in the clamps.



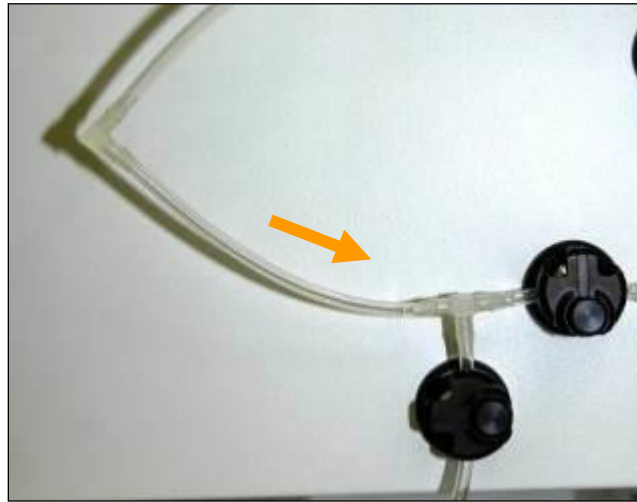
4. Install the tubing between the mixing and separation bag into V10, aligning black mark on tubing to be above the pinch valve as shown.



5. Install the separation bag on the face of the device at load cell 6. Confirm that the tube entering the separation bag is routed loosely as shown.

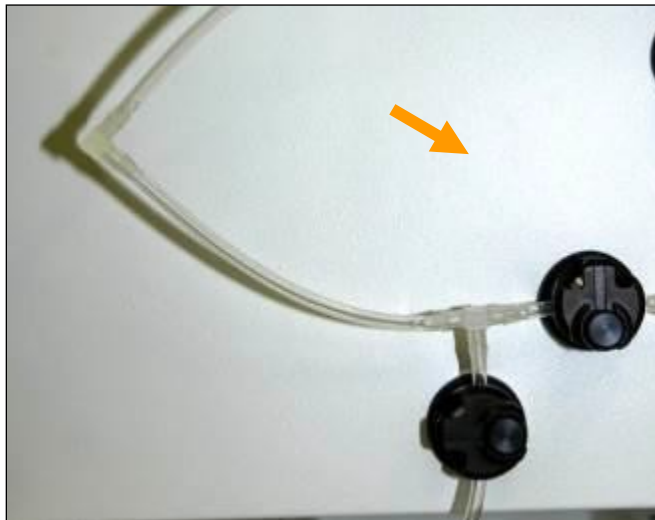


6. Route the tubing below the separation bag and install into V7.

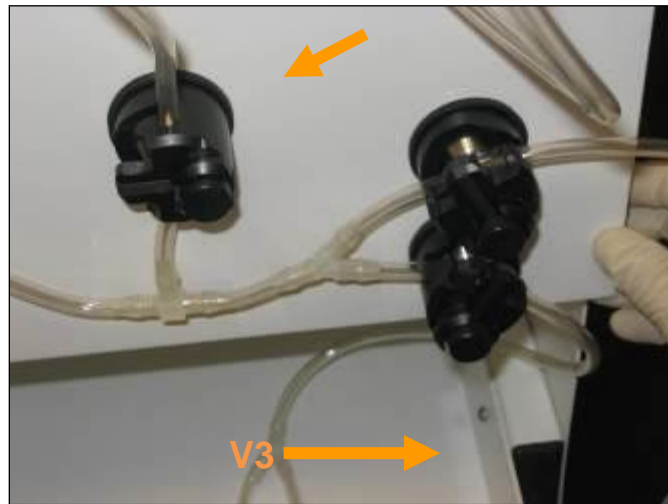


7. Place the solvent waste bag in the bottom tray of the device.

8. Install the tubing before the next "T" into V1.

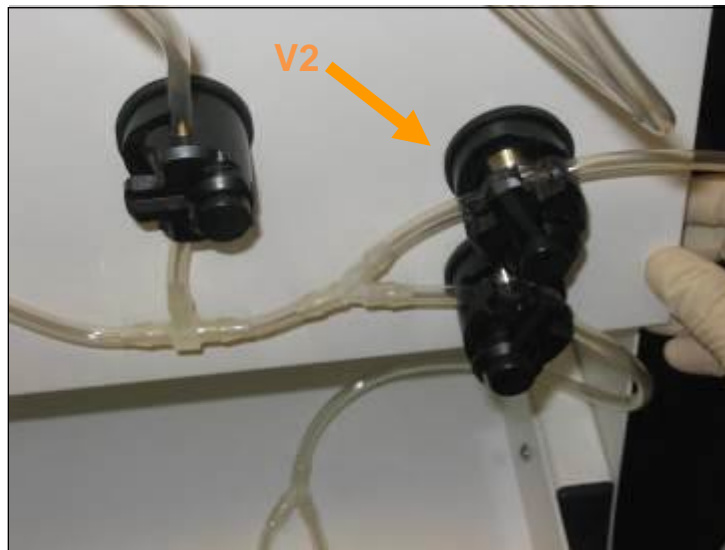


9. Install the branch of the “T” without a “Y” into V6.



10. Install the branch of the “Y” with only one tube into V2.

11. Install the branch of the “Y” with another “Y” into V3.



12. Connect the priming connector tube at the DIN connector above V6 and mount it into

the upper and lower column clamp slots.



13. Install the tubing above the priming connector tube into the peristaltic pump.

14. Close the pump clamp.



15. Install the right branch of the “T” above the pump leading the prime waste bag into V5.



16. Mount the prime waste bag on the posts on the right side of the device.



17. Install the other branch of the “T” into V4 (Output Plasma valve).

18. Conduct a final inspection for kinks, or damage to the tubing set. Verify that tubes are properly flossed into valves and clips and that the bags are hanging properly on their posts.

19. If no problems with disposables installation, press "Ok" to the prompt dialog. All ten valves will close.
20. Hang the Output Plasma bag on LC5 above valve V4.
21. Remove and discard the cap from the female spike port on the tubing set leading to the output bag.
22. Using appropriate aseptic technique, spike the spike port with the output plasma bag spike.

9.3 Spike Solutions

All ten valves are now closed and you will be prompted to load the consumables as shown in Figure 11.

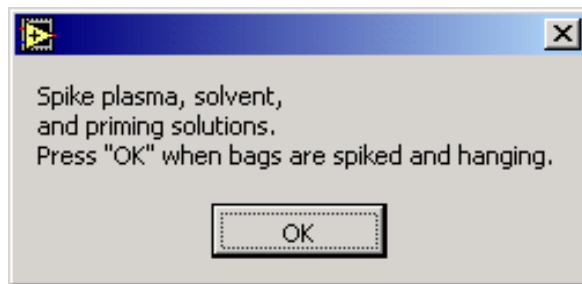


Figure 11: Prompt to spike consumables.

Using appropriate aseptic technique, spike the input plasma and the three saline bags.

Caution
Use care in spiking the plasma bag so as to avoid injury or biohazard exposure

The input plasma hangs on LC1. Hang the three saline bags; one on LC3 and two on LC4. Connect the Solvent-In bag to the Luer above V9 and hang it on LC2.

Use appropriate aseptic technique.

Warning
Failure to use appropriate aseptic technique may result in plasma contamination

Confirm that all disposable tubing set clamps are open or that they have been removed from the tubing set.

Figure 12 shows the disposable tubing set that is fully installed on the device (note that charcoal column is not yet installed). The system is ready to begin the priming and delipidation process.



Figure 12: Disposable and consumables loaded on the system

11. Priming the Disposable Set

10.1 Starting the Process

Once the disposable tubing set and the consumable fluid bags are fully installed, press “OK” on the prompting dialog shown in Figure 11.

10.2 Priming the Tubing Set

The first step in the delipidation process is to prime the tubing set with saline. This minimizes the introduction of air into the solvent removal column.

Do not handle or touch the bags or tubing while the device is operating. Process parameters may be disrupted.

Warning
Do not handle the bags or tubing during operation.

10.3 Monitoring Priming

The Status window provides information about the current state of the machine. It will instruct the operator how the process is proceeding.

The blue progress bar shows progress toward completion of each stage of the process. See Figure 13.

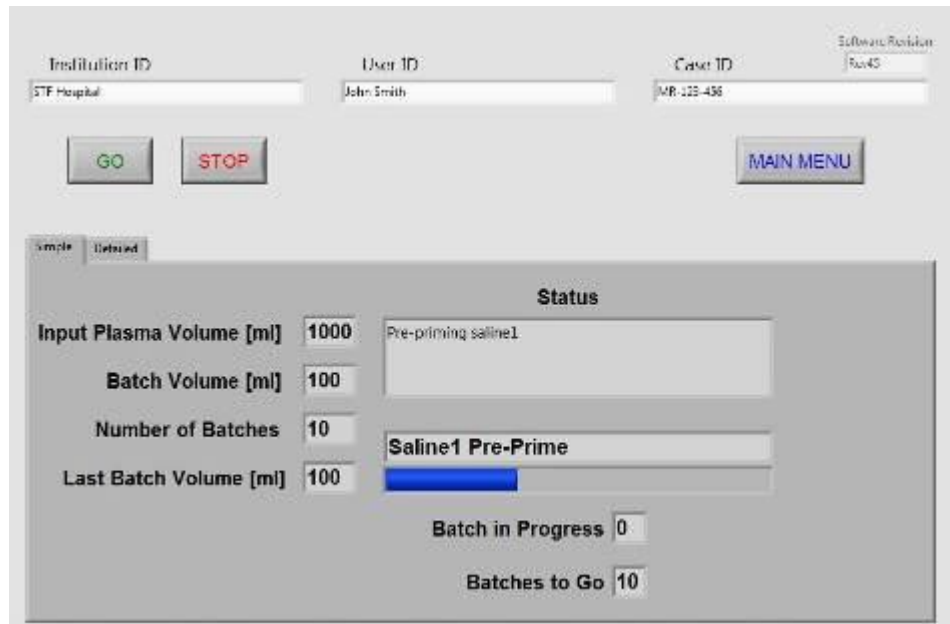


Figure 13: Delipidation screen showing status window and progress bar

10.4 Installing the Solvent Removal Column

After the tubing set is primed, a dialogue box will appear requesting the installation of the column (Figure 14). Do not select “OK” until column is installed.

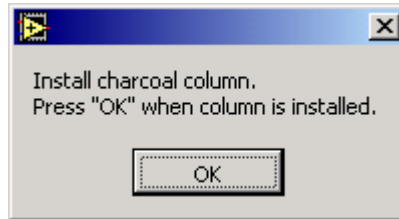


Figure 14: Prompt to install charcoal column

Install the solvent removal column by performing the following steps:

1. Apply a hemostat to the middle of the priming connector tube that connects the entry and exit ports on the tubing set for the column. This will prevent fluid from leaking from the tube when it is disconnected. Disconnect the priming connector tube, remove the hemostat, and discard the tube.

Note: At this point, visually inspect the column for damage, and do not use a previously used column.

2. Hold the column upside down (see Figure 15a).



Figure 15a: Installing the Solvent Removal Column (bottom first)

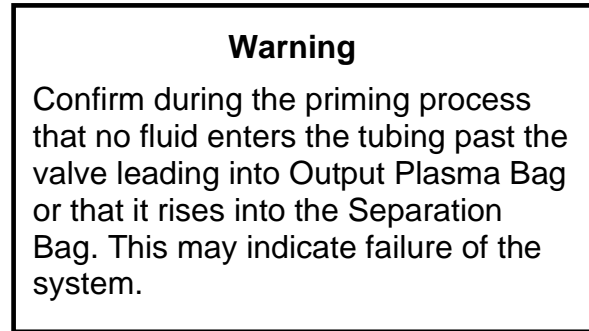
3. Remove the cap on the end and discard.
4. Twist on the DIN connector of the tubing set that leads down toward the bottom of the device. Be sure to make a firm connection.
5. Turn the column right side up.
6. Remove the cap on the other end and discard.
7. Twist on the DIN connector of the tubing set that leads up toward the top of the device. Be sure to make a firm connection.
8. Install the column in the bracket mounted to the face of the instrument.
9. Inspect the installation and confirm that the flow direction arrows point upwards (see figure 15b), and then press “OK” on the prompting dialog (Figure 14).



Figure 15b: Confirmation of column installation in bracket

10.5 Priming the Solvent Removal Column

After the operator presses “OK” on the dialog, the pump runs to prime the column with saline. This rinses the column and prepares it to receive plasma.

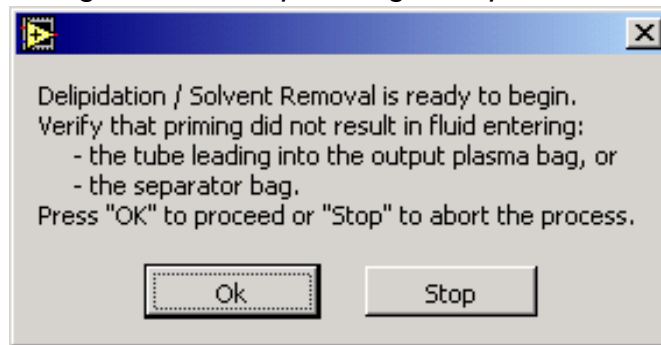


12. Delipidation

Please note that therapy session with the PDS-2 System is limited to seven weekly treatments.

After priming, the system prompts to user to confirm that delipidation may begin (Figure 16). Press “OK” to begin delipidation.

Figure 16: Prompt to begin delipidation



Delipidation is fully automated and does not need any operator participation or intervention. The status window will show the progress of each step. The process takes about four hours.

11.1. Monitoring Delipidation

The Status Window provides information about the current state delipidation (see Figure 17). The progress bar will continue to keep the user informed of progress during each stage to completion.

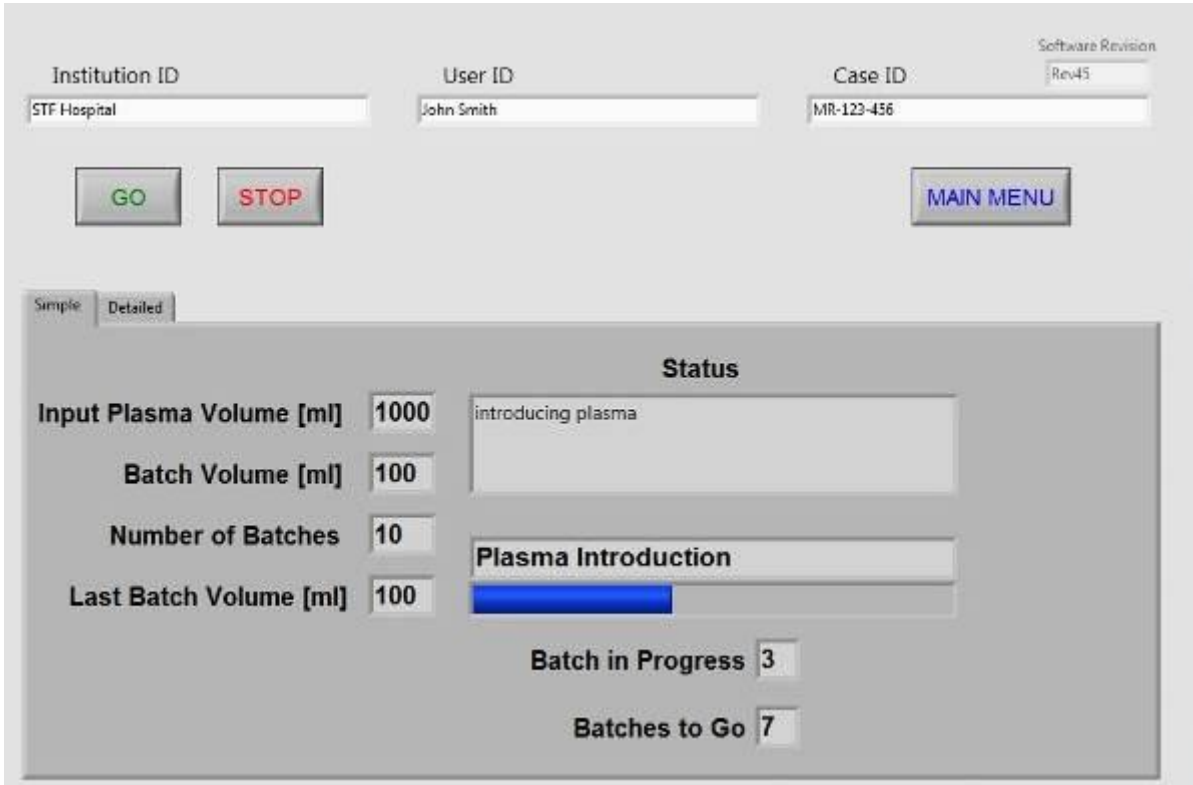



Figure 17: Screen showing status of delipidation

Note: Inspect bags visually during delipidation to ensure there has been no loosening of connections due to vibration of mixer platform.

Note: Do not handle or touch the bags or tubing while the device is operating to avoid disrupting process parameters.

Warning
Do not handle the bags or tubing during operation

Warning

 Keep fingers away from mixing platform to avoid potential pinching hazard

13. Removing the Tubing Set

When the process is complete, the operator will be prompted to disconnect the output plasma bag and to choose an unloading option for the disposable.

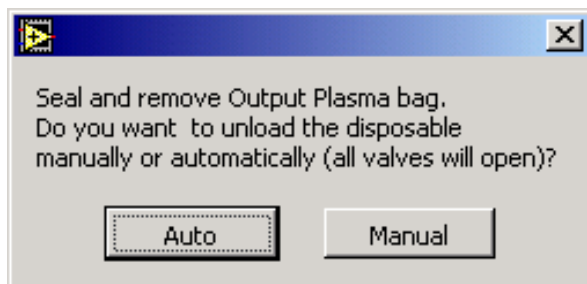


Figure 18: Prompt to seal output bag and choose unloading option

Observing appropriate aseptic technique, seal the output plasma bag with a tube sealer and separate it from the disposable. Put the output plasma aside.

Warning
Failure to use appropriate aseptic technique may result in plasma contamination.

Note: Be sure that the output plasma bag has been sealed and removed before selecting this option.

To open all the valves to remove the disposable, select “Auto” in the dialog of Figure 18. All ten valves will open immediately. Allow the fluid to drain into the waste bags.

To keep the valves closed, and manually remove the disposable from each valve, select “Manual.” The system will end the process and return to the Main Menu.

The tubing set can be separated into three distinct pieces: the solvent waste bag, the prime waste bag, and the combination of the column, separation bag, plasma bag, solvent bag, and the tubing that connects them.

Remove the disposable tubing set according to the following steps (see Figure 19 below):

1. Close all thumb clamps.
2. Disconnect the Luer fitting of the solvent waste bag and dispose according to your institution's chemical waste disposal protocols.
3. Disconnect the Luer fitting of the prime waste bag and dispose according to your institution's biohazardous waste protocol.
4. Remove the tubing from V8 and V9.
5. Remove the mixing bag from the platform.
6. Remove the tubing from V10.
7. Remove the tubing from V1 and V7.
8. Remove the tubing from V2 and V3.
9. Remove the tubing from V5 and V6.
10. Remove the tubing from the pump.
11. Remove the tubing from V4.
12. Collect the hanging bags from each of their respective load cells.
13. The tubing set with the remaining connected hanging bags is now ready to be disposed of according to your institution's biohazardous and/or chemical waste protocols.

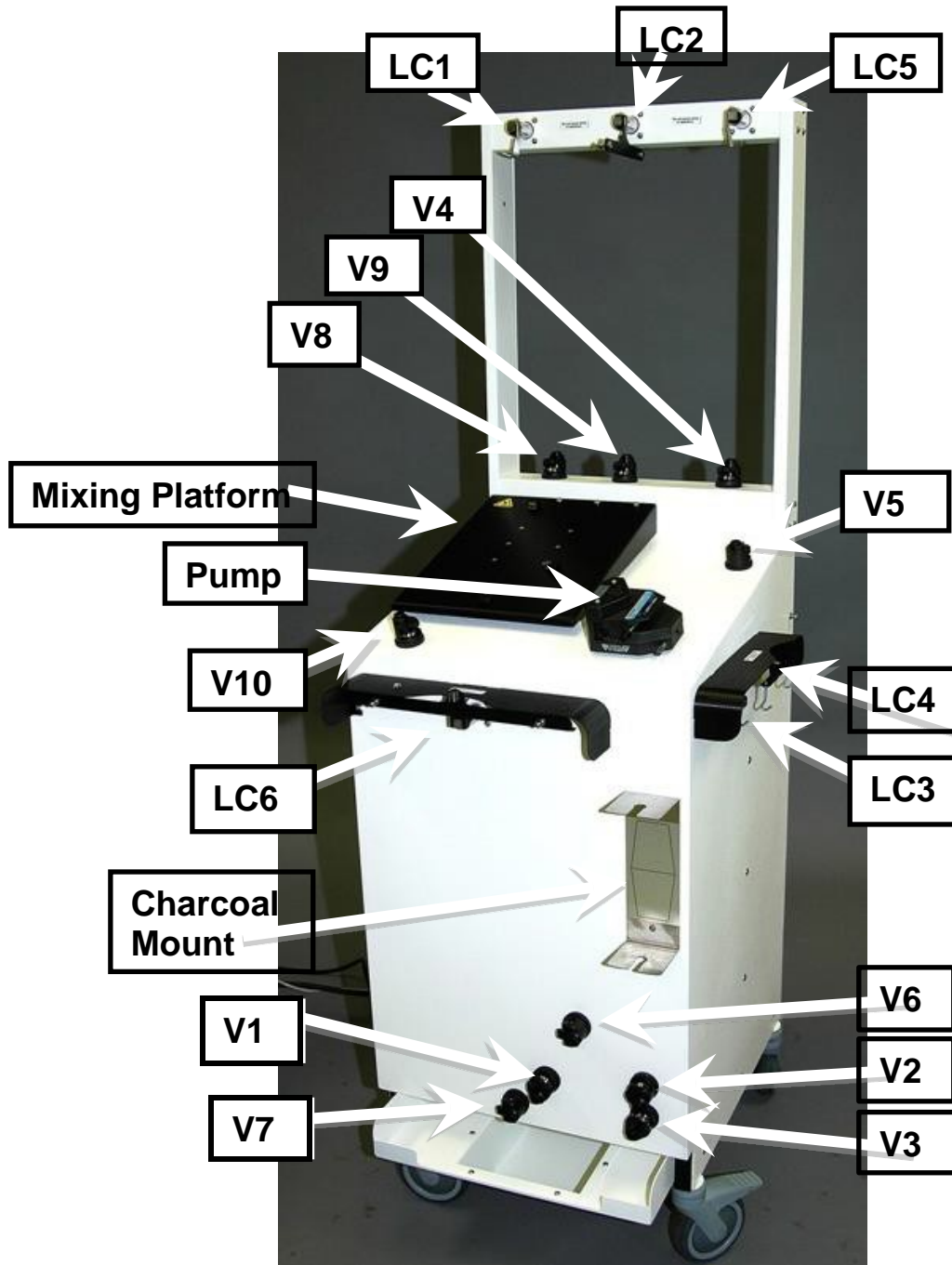


Figure 19: Locations of Major Components on Device

14. Reinfusion of Delipidated Plasma

Verify system performed as specified prior to reinfusion of delipidated plasma. Reinfusion should begin within one hour of completion of the delipidation process. Reinfusion should be conducted using standard reinfusion techniques, per the reinfusion system Instructions for Use and hospital standard processes for reinfusion. Delipidated plasma should be kept at room temperature. Monitor patient for signs of solvent toxicity, hypoglycemia, and hypocalcemia during and after reinfusion.

15. Shutting the System Down

If the “Manual” option was chosen to unload the disposable tubing set, the PC will shut down when the “Manual” option is selected.

If the “Auto” option was chosen to unload the disposable tubing set, select “OK” after the disposable tubing set is unloaded, and the PC will shut down.


Turn off the power of the instrument. The power switch is located on the left side near the bottom.


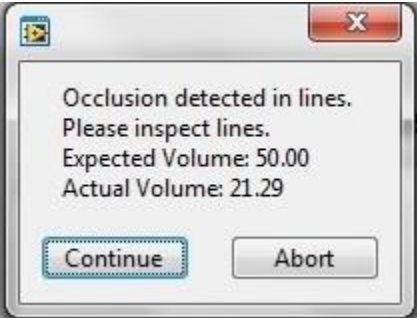
Turn off the power of the monitor.

Note: Always shut down the system completely after completing a delipidation process. Do not start another delipidation process without first shutting the system down.

16. Troubleshooting

Attention: Always turn off instrument and console before checking cable connections.

Symptom	Cause	Action
Console screen is black	Screen save active	Move the mouse
	Monitor switched off	Turn on the monitor
	Cable to monitor unplugged	Check monitor cable
	Computer is switched off	Turn on computer
Console screen shows “Windows Error Recovery” display when system is powered on 	System was not shut down normally following previous use	Press “Enter” Key on PC Keyboard to Start Windows normally

Symptom	Cause	Action
<p>Console screen shows “Windows has recovered from an unexpected shutdown” display when system is powered on</p> 	<p>System PC had an error occur during previous use</p>	<p>Press “Cancel” Key on Console screen using mouse to resume Windows</p>
<p>Console screen shows “Occlusion detected In lines” message</p> 	<p>Twist or kink in tubing</p>	<p>Inspect tubing and adjust tubing to eliminate twists or kinks. Select “Continue” from message window.</p> <p>If “Occlusion detected in lines” message still re-appears after three attempts to clear an occlusion, select “Abort” from the Occlusion message window and proceed to the “Stopping” sections for instructions</p>

Console screen shows error messages regarding Pump and/or DAQmx soon after pressing the “GO” button when starting the delipidation process

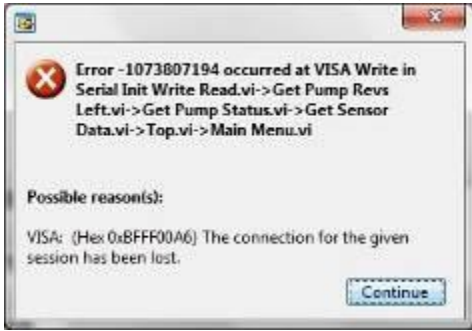


Sample error messages:



PDS-2 Instrument is switched off

1. Press and hold PC Power button for 10 seconds.
2. Release PC Power button and wait for 30 seconds.
3. Press PC Power button to re-start system
4. Turn PDS-2 Instrument ON
5. Console screen will show “Windows Error Recovery” display. Press “Enter” key on PC keyboard to “Start Windows Normally
6. When prompted, enter the correct username and password, and click on “OK” when completed. Main Menu will appear.
7. Restart process from Step 8.5 “Main Menu” in this Manual

Symptom	Cause	Action
	PDS-2 Instrument power cord unplugged	Check PDS-2 Instrument power cable, then follow Steps 1-7 above
	Blown mains fuse in PDS-2 Instrument	Check PDS-2 Instrument mains fuse, then follow Steps 1-7 above
	USB Data cable unplugged (DAQmx communications)	Check USB Data cable, then follow Steps 1-7 above
	USB to RS-232 cable unplugged (Pump communications)	Check USB to RS-232 cable, then follow Steps 1-7 above

Symptom	Cause	Action
<p>Console screen shows error messages regarding Pump or DAQmx, or Blue Screen during delipidation process</p> <p>Sample error messages:</p>   	<p>PDS-2 Instrument power cord unplugged</p> <p>Blown mains fuse in PDS-2 Instrument</p> <p>USB Data cable unplugged (DAQmx communications)</p> <p>USB to RS-232 cable unplugged (Pump communications)</p> <p>PC Failure</p>	<ol style="list-style-type: none"> 1. Shut off PDS-2 Instrument using power switch on left side of Instrument 2. Press and hold PC Power button for 10 seconds. 3. The delipidation in progress cannot be resumed. Uninstall the disposable and fluids, and dispose of as described in the section above on Removing the Tubing set. 4. All liquids and plasma are to be disposed of according to your institution's biohazardous and/or chemical waste protocols
<p>Solvent bag exhausted</p>	<p>More dispensed than expected</p>	<p>Abort process</p>

Symptom	Cause	Action
Plasma drained to waste during bulk solvent removal	Load cell interference	Do not touch the load cells during operation
Pump rate too fast or too slow and pump stops	Pump calibration incorrect	Contact HDL for system recalibration

13.1 Stopping

If necessary, a delipidation in progress can be stopped by clicking the large red “Stop” button in the middle of the control Interface on the console application or by selecting “Abort” or “Stop” in a message window. The following actions are performed:

- The pump is stopped
- All the valves are closed
- The message “Premature end” will appear in the status window

The delipidation in progress cannot be resumed.

Remove the tubing set according to the instructions in the “Removing the Tubing Set” section.

The system will return to the Main Menu.

The Shutdown option must be chosen from the Main Menu to shut down the PC.

Turn off the power of the instrument. The power switch is located on the left side near the bottom.

Note: Always shut down the system power after stopping a delipidation process. Do not start another delipidation process without first shutting the system down.

If the delipidation process is stopped for any reason, the plasma cannot be recovered. Plasma should be discarded. Uninstall the disposables and fluids, and dispose of as described in the section above on removing the tubing set.

Note: If the process is interrupted, such as by loss of power, the delipidation in progress cannot be resumed, and disposables, consumables, and plasma must be discarded.

17. Service and Repair

Besides the fuses noted below, there are no user-serviceable parts on the system. If the operation cannot be restored by completing the suggestions in the “Troubleshooting” section of this manual, the system should be serviced by HDL Therapeutics personnel.

The useful life of the device is estimated at 2 years, assuming normal use, and that recommended, care, maintenance, and service and maintenance are performed.

18. Care and Maintenance

132 Cleaning and Disinfection

The PDS-2 System should be cleaned immediately after each procedure. All surfaces of both the instrument and the computer console may be cleaned/disinfected with EPA listed/CDC Recommended Hospital Grade Cleaning/Disinfectant Wipes (e.g. CaviWipes™, CaviWipes1™, MadaCide-FDW-Plus™),

Cleaning Instructions

- Disconnect and takedown used tubing and disposables from the PDS-2 instrument.
- Discard tubing and single-use disposables in appropriate leak-proof biohazardous waste container.
- Check for visible soil or plasma on instrument surfaces.
- Apply cleaning wipes (e.g., CaviWipes™) to thoroughly clean all soiled surfaces of the device using a wiping motion with friction. Ensure surfaces are visibly wet with disinfectant.
- The cleaning solution should be in contact with the device for at least three minutes at ambient room temperature.
- Sufficient number of wipes should be used to thoroughly clean all soiled surfaces.
- Allow surfaces to air dry.
- Clean *before* disinfecting with solution/wipe noted above.
- Inspect the device after cleaning for any soil that may remain. Repeat cleaning steps if any visual soil remains.
- Discard all single-use supplies.
- Remove gloves and perform hand hygiene.

Routine Disinfection Instructions

- Wear clean gloves.
- Disinfect *after* cleaning with solution/wipe noted above.
- Apply disinfectant wipes (e.g., CaviWipes™) to thoroughly disinfect all surfaces of the PDS-2 instrument using a wiping motion (with friction). Ensure surfaces are visibly wet with disinfectant.
- The disinfectant should be in contact with the device for at least three minutes at ambient room temperature.
- Sufficient number of wipes should be used to thoroughly disinfect all surfaces.
- Allow surfaces to air-dry.
- Remove gloves and perform hand hygiene.

13.3 Spills

Should a spill of treated or untreated plasma or solvents occur, clean and dispose of the spill components as required by the institution's chemical and/or biohazard procedures. Ensure that PDS-2 System is subsequently cleaned and disinfected per 17.1.

13.4 Storage

17.3.1 System

The device and console should be turned off and unplugged from the AC mains for storage. The cables that connect the two parts may remain connected. Disconnect all cables if storing for extended periods.

17.3.2 Supplies

Sealed disposable sets should be stored away from direct exposure to light. Expired sets should be discarded in accordance with the disposal protocols of your institution.

17.4 Installation Qualification (IQ)

The system will be installed by HDL trained technicians in accordance with the installation manual. A record of the installation and IQ results will be generated and maintained.

17.5 Preventive Maintenance

Check the instrument to be sure that preventive maintenance has been performed within the last 12 months by HDL Therapeutics personnel to

assure device continues to operate properly.

19. Disposal

Risks associated with disposal of medical disposables

Medical wastes, including disposables used in the delipidation process, are considered biohazardous materials. Failure to properly dispose of these materials can potentially cause exposure to infectious diseases.

Properly dispose of medical waste in accordance with authorized laboratory practices, and in accordance with local, state, and federal regulations for medical waste.

Risks associated with disposal of product at end of useful life

The PDS-2 Delipidation system is an electronic product. Risks associated with improper disposal of the PDS-2 Delipidation system at the end of its useful product life includes potential environmental hazards.

When this product is to be disposed of, follow authorized laboratory practices, including local, state, and federal regulations for WEEE (Waste Electrical and Electronic Equipment).

20. Additional Parts/Materials List

Fuses (2):

120VAC System

8 Amp Slow Blow T8A250V (qty. 2)

230VAC System

8 Amp Slow Blow T8A250V (qty. 2)

Consumables:

0.9% NaCl Injection, USP, 1L x 3 Baxter P/N 2B1324
or equivalent

Bags:

Input Plasma Bag, 1L with needle connector Baxter P/N 4R2247
Or equivalent

Output Plasma Bag, 2L with coupler Baxter P/N 4R2041
or equivalent

21. Specifications

Physical (PDS-2) Instrument Height:

64 inches

Width: 24 inches

Depth: 28 inches

Weight: 203 lbs.

Environmental Requirements:

Operating: Temperature: 15 to 30 °C
 Humidity: 10 to 90% RH (non-condensing)
 Altitude: up to 1600 meters

Shipping: Temperature: -20 to 60 °C
 Humidity: 20 to 75% RH (non-condensing)
 Altitude: up to 2,000 meters

Storage: Temperature: -20 to 60 °C
 Humidity: 20 to 75% RH (non-condensing)
 Altitude: up to 2,000 meters

Incline: up to 10° incline from level

Power Requirements

120 VAC 60 Hz 240 VA (US) or 230 VAC 50Hz 240VA (EU)
Maximum Power: 350 watts
Nominal Power: <200 watts
Fuse Rating Mains: 8A Slow-Blow (US) and (EU)

Battery Specification Information: An Uninterruptible Power Supply (UPS) is used to power the system for up to 30 minutes after a power loss.

22. Symbols

If applicable, the following symbols may appear on the PDS-2 device.



Indicates that consultation of the accompanying documents prior to equipment operation is critical to the safe operation of the device.



Indicates that the device requires an alternating supply current.



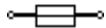
Indicates the location of USB data connection on instrument.



Indicates the location of the USB to RS-232 converter cable connection on instrument.















Indicates potential pinch point.













Indicates device contains a fuse which disconnects when current is above threshold.

If applicable, the following symbols may appear on the PDS-2 disposables.

SYMBOL	DESCRIPTION
	<p>Indicates the need for the user to consult the instructions for use for important cautionary information such as warnings and precautions that cannot, for a variety of reasons, be presented on the medical device itself.</p>
	<p>Indicates the manufacturer's batch code so that the batch or lot can be identified.</p>
	<p>Indicates a medical device that is intended for one use, or for use on a single patient during a single procedure.</p>
	<p>Indicates the manufacturer's catalogue number so that the medical device can be identified.</p>

SYMBOL	DESCRIPTION
	<p>Indicates a medical device that has been sterilized using irradiation.</p>
	<p>Indicates the date after which the medical device is not to be used.</p>
	<p>Indicates a medical device that is non-pyrogenic.</p>
	<p>Indicates the range of atmospheric pressure to which the medical device can be safely exposed.</p>
	<p>Indicates the need for the user to consult the instructions for use.</p>
	<p>Indicates the humidity limits to which the medical device can be safely exposed.</p>
	<p>Indicates the temperature limits to which the medical device can be safely exposed.</p>
	<p>Indicates the Authorized Representative in the European Community.</p>

SYMBOL	DESCRIPTION
	<p>Indicates the presence of a fluid path.</p>
	<p>Indicates the medical device manufacturer, as defined in EU Directives 90/385/EEC, 93/42/EEC and 98/79/EC.</p>
	<p>Indicates the presence of a sterile fluid path within the medical device in cases when other parts of the medical device, including the exterior, might not be supplied sterile.</p>
	<p>Indicates a medical device that should not be used if the package has been damaged or opened.</p>
	<p>Indicates a medical device that is not to be resterilized.</p>
	<p>Indicating that that the device requires an alternating supply current</p>
	<p>Indicating that the device has a protective earth ground</p>
	<p>Indicates that the product is a prescription medical device</p>

	<p>Indicates product that does contain the phthalate plasticizer DEHP.</p>
	<p>Indicates main power is turned off/on</p>

23. Certifications

1. This device is classified as Class I (via ground) per EN 60601-1 for electrical safety, with no connection to the patient. This classification is based on the degree of protection afforded against electrical shock, as defined in these standards.
2. This device has Ordinary Protection for Fluid Ingress IPX 0 per IEC 60529.
3. This equipment is suitable for continuous operation.

24. Electromagnetic Compatibility User Information

The EMC tables and other guidelines that are included in this Operator's Manual provide information to the customer or user that is essential in determining the suitability of the Equipment or System for the Electromagnetic Environment of use, and in managing the Electromagnetic Environment of use to permit the Equipment or System to perform its intended use without disturbing other Equipment and Systems or non-medical electrical equipment.

1. Electromagnetic Emissions

WARNING: Medical electrical equipment needs special precautions regarding Electromagnetic Compatibility (EMC) and needs to be installed and put into service according to the EMC information provided in this manual.

WARNING: Use of this equipment adjacent to or stacked with other equipment should be avoided because it could result in improper operation. If such use is necessary, this equipment and the other equipment should be observed to verify that they are operating normally.

WARNING: The use of accessories, transducers, and cables other than those specified or provided by HDL Therapeutics, Inc. could result in increased electromagnetic emissions or decreased electromagnetic immunity of this equipment and result in improper operation.

WARNING: Portable RF communications equipment (including peripherals such as antenna cables and external antennas) should be used no closer than 30 cm (12 inches) to any part of the PDS-2 System, including cables specified by the manufacturer. Otherwise, degradation of the performance of this equipment could result.

NOTE: *The EMISSIONS characteristics of this equipment make it suitable for use in industrial areas and hospitals (CISPR 11 class A). If it is used in a residential environment (for which CISPR 11 class B is normally required) this equipment might not offer adequate protection to radio-frequency communication services. The user might need to take mitigation measures, such as relocating or re-orienting the equipment.*

**Guidance and Manufacturer's Declaration – Emissions
All ME Equipment and ME Systems**

The PDS-2™ is intended for use in the electromagnetic environment specified below. The customer or user of the PDS-2™ should assure that it is used in such an environment.

Emissions Test	Compliance	Electromagnetic Enforcement – guidance
RF Emissions CISPR 11	Group 1	The PDS-2™ uses RF energy only for its internal function. Therefore, its RF emissions are very low and are not likely to cause any interference in nearby electronic equipment.
RF Emissions CISPR 11	Class A	The PDS-2™ is suitable for use in all establishments other than domestic and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes.
Harmonics IEC 61000-3-2	Class A	
Flicker IEC 61000-3-3	Complies	

2. Electromagnetic Immunity

Guidance and Manufacturer's Declaration – Immunity All ME Equipment and ME Systems			
The PDS-2™ is intended for use in the electromagnetic environment specified below. The customer or user of the PDS-2™ should assure that it is used in such an environment.			
Immunity Test	IEC 60601 Test Level	Compliance Level	Electromagnetic Environment – Guidance
Electrostatic Discharge (ESD) IEC 61000-4-2	±8 kV Contact ±2 kV, ±4 kV, ±8 kV, ±15 kV Air	±8 kV Contact ±2 kV, ±4 kV, ±8 kV, ±15 kV Air	Floors should be wood, concrete or ceramic tile. If floors are synthetic, the relative humidity should be at least 30%.
Electrical Fast Transient (EFT) IEC 61000-4-4	±2 kV Mains ±1 kV I/Os	±2 kV Mains ±1 kV I/Os	Mains power quality should be that of a typical commercial or hospital environment.
Surge IEC 61000-4-5	±1 kV Differential ±2 kV Common	±1 kV Differential ±2 kV Common	Mains power quality should be that of a typical commercial or hospital environment.
Voltage Dips and Dropouts IEC 61000-4-11	0% U _T ; 0,5 cycle At 0°, 45°, 90°, 135°, 180°, 225°, 270° and 315° 0% U _T ; 1 cycle and 70% U _T ; 25/30 cycles Single phase: at 0° 0% U _T ; 250/300 cycles	0% U _T ; 0,5 cycle At 0°, 45°, 90°, 135°, 180°, 225°, 270° and 315° 0% U _T ; 1 cycle and 70% U _T ; 25/30 cycles Single phase: at 0° 0% U _T ; 250/300 cycles	Mains power quality should be that of a typical commercial or hospital environment. If the user of the PDS-2™ System requires continued operation during power mains interruptions, it is recommended that the PDS-2™ System be powered from an uninterruptible power supply or battery.
Power Frequency 50/60 Hz Magnetic Field IEC 61000-4-8	30 A/m	30 A/m	Power frequency magnetic fields should be that of a typical commercial or hospital environment.

**Guidance and Manufacturer's Declaration – Immunity
ME Equipment and ME Systems that are NOT Life-Supporting**

The PDS-2™ is intended for use in the electromagnetic environment specified below. The customer or user of the PDS-2™ should assure that it is used in such an environment.

Immunity Test	IEC 60601 Test Level	Compliance Level	Electromagnetic Environment –
Conducted RF IEC 61000-4-6	3V 0.15 MHz – 80 MHz 6V in ISM (industrial, scientific and medical) bands between 0.15 MHz and 80 MHz 6V in amateur radio bands between 0.15 MHz and 80 MHz 80% AM at 1 kHz	3V 0.15 MHz – 80 MHz 6V in ISM (industrial, scientific and medical) bands between 0.15 MHz and 80 MHz 6V in amateur radio bands between 0.15 MHz and 80 MHz 80% AM at 1 kHz	PROFESSIONAL HEALTHCARE FACILITY ENVIRONMENT
Radiated RF IEC 61000-4-3	3 V/m 80 MHz – 2.7 GHz 80% AM at 1 kHz	3 V/m 80 MHz – 2.7 GHz 80% AM at 1 kHz	PROFESSIONAL HEALTHCARE FACILITY ENVIRONMENT

NOTE 1 At 80 MHz and 800 MHz, the higher frequency range applies.

NOTE 2 These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.

- The ISM (industrial, scientific and medical) bands between 150 kHz and 80 MHz are 6,765 MHz to 6,795 MHz; 13,553 MHz to 13,567 MHz; 25,957 MHz to 27,283 MHz; and 40,66 MHz to 40,70 MHz.
- The compliance levels in the ISM frequency bands between 150 kHz and 80 MHz and in the frequency range 80 MHz to 2.5 GHz are intended to decrease the likelihood that mobile/portable communications equipment that could cause interference if it is inadvertently brought into patient areas. For this reason, an additional factor of 10/3 has been incorporated into the formulae used in calculating the recommended separation distance for transmitters in these frequency ranges.
- Field strengths from fixed transmitters, such as base stations for radio (cellular/cordless) telephones and land mobile radios, amateur radio, AM and FM radio broadcast and TV broadcast cannot be predicted theoretically with accuracy. To assess the electromagnetic environment due to fixed RF transmitters, an electromagnetic site survey should be considered. If the measured field strength in the location in which the PDS-2™ is used exceeds the applicable RF compliance level above, the PDS-2™ should be observed to verify normal operation. If abnormal operation is observed, additional measures may be necessary, such as re-orienting or relocating the PDS-2™.
- Over the frequency range 150 kHz to 80 MHz, field strengths should be less than 1 V/m.

3. Immunity to RF Wireless Communications Equipment

Guidance and Manufacturer's Declaration — Immunity ME Equipment and ME Systems that are NOT Life-Supporting						
The PDS-2™ System is intended for use in the electromagnetic environment specified below. The customer or the user of the PDS-2™ System should ensure that it is used in such an environment.						
Test Frequency	Band ¹	Service ¹	Modulation ²	Maximum Power	Distance	Immunity Test Level
MHz	MHz			W	Meters	(V/m)
385	380 – 390	TETRA 400	Pulse modulation ² 18 Hz	1.8	0.3	27
450	430 – 470	GMRS 460, FRS 460	FM ³ ±5 kHz deviation 1 kHz sine	2	0.3	28
710 745 780	704 – 787	LTE Band 13, 17	Pulse modulation ² 217 Hz	0.2	0.3	9
810 870 930	800 – 960	GSM 800/900, TETRA 800, iDEN 820, CDMA 850, LTE Band 5	Pulse modulation ² 18 Hz	2	0.3	28
1720 1845 1970	1700 – 1900	GSM 1800; CDMA 1900; GSM 1900; DECT; LTE Band 1, 3, 4, 25; UMTS	Pulse modulation ² 217 Hz	2	0.3	28
2450	2400 – 2570	Bluetooth, WLAN, 802.11 b/g/n, RFID 2450, LTE Band 7	Pulse modulation ² 217 Hz	2	0.3	28
5240 5500 5785	5100 – 5800	WLAN 802.11 a/n	Pulse modulation ² 217 Hz	0.2	0.3	9

NOTE: If necessary to achieve the IMMUNITY TEST LEVEL, the distance between the transmitting antenna and the PDS-2™ System may be reduced to 1 m. The 1 m test distance is permitted by IEC 61000-4-3.

¹ For some services, only the uplink frequencies are included.

² The carrier shall be modulated using a 50% duty cycle square wave signal.

³ As an alternative to FM modulation, 50% pulse modulation at 18 Hz may be used because while it does not represent actual modulation, it would be worst case.

4. Essential Performance

Our System's essential performance has been identified as follows:

- Requires that control of the pump flow rate is maintained to identify levels so that the solvent that may still be remaining in the plasma after gravity separation is not returned to the patient.
- The error messages or blank screens that appeared after the Electrostatic Discharge (ESD) test events identifies to the operator that the process has failed.
- In the event of error message that are unrecoverable or the system becomes non-responsive, our Instructions for Use instructs the operator to discard the materials in process and terminate the delipidation process, ensuring that plasma that may contain excessive solvent is not returned to the patient.

25. APPENDIX 1: SOLVENT MIXING PROCESS

1. Equipment, Materials and Process Summary

a. Preparer, equipment: The preparer shall ensure that the following equipment are available and functioning properly, and that the required materials are available before solvent mixing is conducted:

- Solvents (Sevoflurane and n-Butanol) in sufficient volume for the final solvent mix
- Solvent Transfer Set
- Solvent In-bag
- Calibrated Masterflex™ pump and Head
- Calibrated Scale (>4Kg capacity)
- Fume Hood
- Biotainer™ container
- Sterile needle (~18ga)
- Sterile pipet and pipet gun
- Clamps, other general supplies

MATERIALS BATCH LIST

Item	Manufacturer	Quantity	Part Number	SN/LN	Calibration Expiry Date
Sevoflurane (250 ml bottle x 9)	Abbott	2250mL	Ultane		
n-butanol	Pharmco	118mL	331USP/NF		
Solvent In-Bag	HMP	1	H148401		
Solvent Transfer Set	HMP	1	H159401		
Scale (4Kg capacity)		1			
Fume Hood		1			
MasterFlex Pump	MasterFlex	1	7524-40		

Easy Load II Pump Head	MasterFlex	1	77201-60		
Disposable 18G Needle	BD	1	305199		
Biotainer HDPE Container	Nalgene	1	3750-24		
Pyrex Disposable Serological Pipet (10mL)	Corning	1	7077-10N		
Disposable Serological Pipet (25mL)	Fisher	1	13-678-36D		
Disposable Serological Pipet (50mL)	Fisher	2	13-678-36E		
Polydisk AS 0.2u filter	Whatman	1	6724-5002		
Pipetman™, Pipet-Aid™ or other pipet gun		1			

2. Prepare Delipidation Solvent Mixture

WARNING

SOLVENT PREPARATION SHOULD ONLY
BE COMPLETED BY TRAINED AND
CERTIFIED PERSONNEL.

WARNING

ASEPTIC TECHNIQUE MUST BE USED
DURING SOLVENT PREPARATION TO
PREVENT CONTAMINATION.

- a. Solvent volume is fixed at nine bottles (2250 mls) of Sevoflurane.
- b. Remove protective wrap from Biotainer™ container and weigh empty container plus cap. Record container weight on Batch Record.
- c. Open and aseptically pour all nine Sevoflurane bottles into the Biotainer. Close cap and weigh Sevoflurane in Biotainer. Record container weight with Sevoflurane on Batch Record.
- d. Subtract container weight from Sevoflurane plus container to obtain weight of Sevoflurane in container.
- e. Calculate volume of Sevoflurane based on Sevoflurane s.g.=1.5225. Record Sevoflurane volume on Batch Record.
- f. Calculate volume of n-butanol required to bring v:v ratio to 95:5 sevoflurane:n-butanol. Record volume of n-butanol on Batch Record.
- g. Open and aseptically attach an appropriately sized sterile pipet to a Pipetman, load the correct amount of n-butanol, remove cap from Biotainer, and add n-butanol to Biotainer.
- h. Close cap tightly, and shake vigorously for about 10 seconds to mix solvent solution.
- i. Check solvent specific gravity. Weigh full container. Subtract container/cap weight and calculate mixed solvent specific gravity based on solvent volumes added. Record on Batch Record.
- j. Complete and sign Solvent-In Bag label set (for appropriate hospital)
- k. Attach one of the two identical labels to the Solvent-In Bag,
- l. Attach the other label to the Batch Record and complete Batch Record.

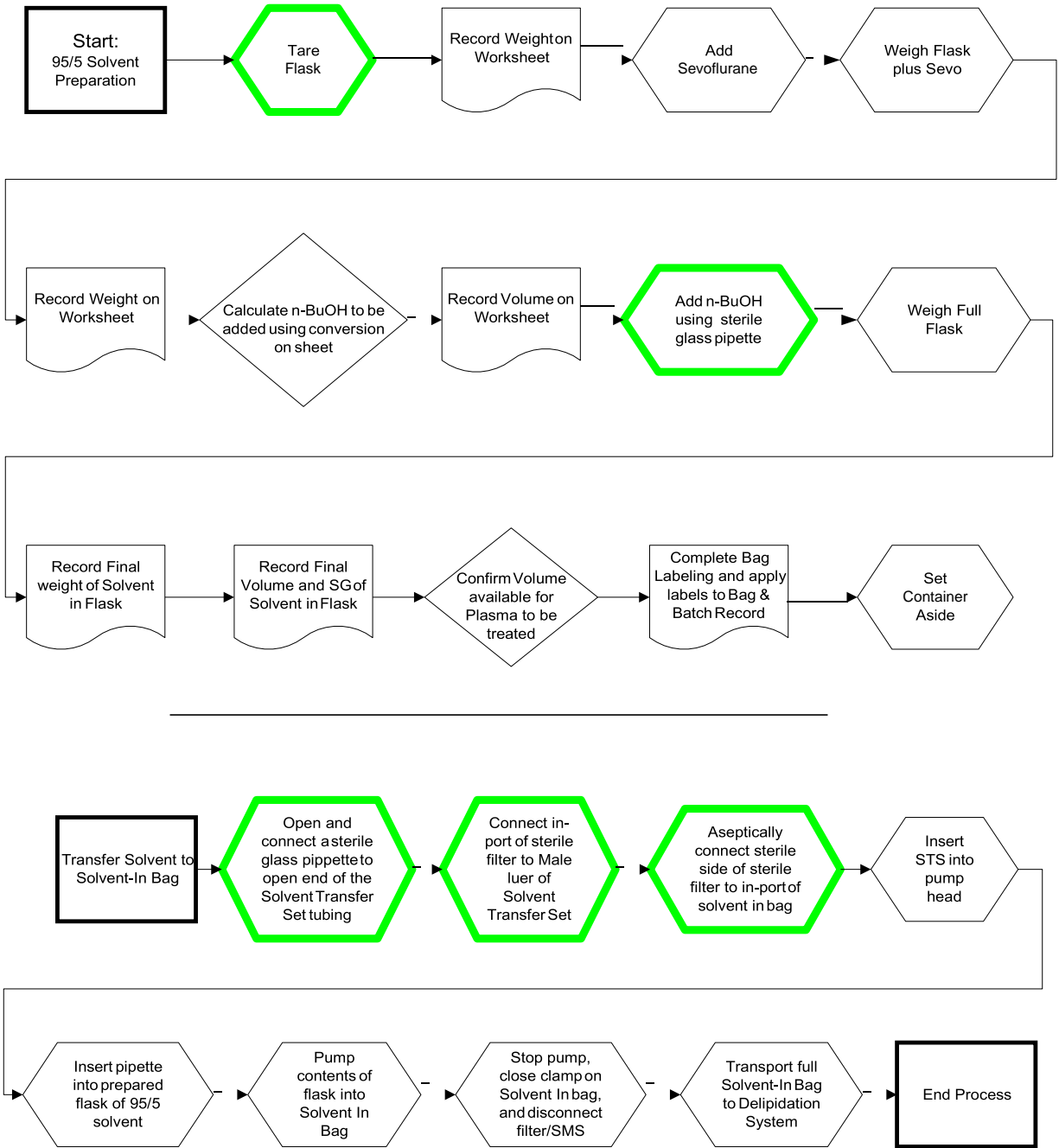
3. Prepare Solvent Transfer Set

- a. Aseptically open end of 10ml pipet and aseptically remove cotton plug with disposable sterile needle.
- b. Open Solvent-Transfer Set, and aseptically insert tip of pipet into end of tubing.
- c. Open 0.2 μ filter and aseptically attach male luer of Solvent-Transfer Set to open barb/luer end of filter.
- d. Remove sterile caps from 0.2 μ filter and inlet (top) port of Solvent-In Bag, and aseptically connect filter outlet to Solvent-In Bag inlet.
- e. Ensure that outlet thumb clamp (bottom) is closed and inlet thumb (top) clamp is open.

4. Transfer Delipidation Solvent Mixture to Solvent-In Bag

- a. Insert tubing into Masterflex pump head.
- b. Set pump to size "16" tubing.
- c. Open solvent container and aseptically insert pipet on assembled Solvent-Transfer Set.
- d. Ensure that thumb clamp is open. Pump solvent at up to 300 ml/min into Solvent-In Bag. Tip container as necessary to pump all solvent from Biotainer into Solvent-In Bag.
- e. Turn pump off, close thumb clamp, and disconnect filter/ Solvent-Transfer Set from Solvent-In Bag. Attach sterile luer plug to inlet (top) port of Solvent-In Bag.

FLOW CHART – SOLVENT PREPARATION PROCESS



CONFIDENTIAL

EXAMPLE SOLVENT PREPARATION BATCH RECORD

(Complete actual Batch Record Form)

- A. Empty tare weight of Biotainer (including cap) = _____g
- B. Weight of Biotainer (including cap) with 9 bottles of sevoflurane added = _____g
- C. Weight of sevoflurane added = B – A= _____g
- D. s.g. sevoflurane = 1.5225 g/ml
- E. Volume of sevoflurane added = $C(g) \div D(g/ml) =$ _____mL
- F. Solvent ratio (v:v) = 5% n-butanol : 95% sevoflurane = (5/95)
- G. Volume of n-butanol to add = $E(ml) \times F =$ _____mL
- H. Total volume of Delipidation Solvent = E+G (ml) = _____ml
- I. Final weight of Delipidation Solvent and Biotainer (including cap) = _____g
- J. Final weight of Delipidation Solvent = I (g) – A (g) = _____g
- K. Final check – S.G. of Delipidation Solvent = $J(g) \div H(ml) =$ _____g/mL
- L. Within acceptable Range 1.4832 - 1.4903 g/mL Yes No (circle one)
- M. Finish: Mix Date ____/____/____ Mix Time ____:____AM / PM (circle one)
- N. Add 36 hours: Expiry Date: ____/____/____ Expiry Time ____:____AM / PM (circle one)
- O. Complete and sign Labeling Set, and attach one label to Solvent-In Bag _____(init)
- P. Attach other label to reverse side of this batch record _____(init)

EXAMPLE COMPLETED SOLVENT PREPARATION BATCH RECORD

(Complete actual Batch Record Form)

- A. Empty tare weight of Biotainer (including cap) = 246.6 g
- B. Weight of Biotainer (including cap) with 9 bottles of sevoflurane added = 3,672.225 g
- C. Weight of sevoflurane added = B – A = 3,672.225 – 246.6 = 3,425.625 g
- D. s.g. sevoflurane = **1.5225** g/ml
- E. *Volume of sevoflurane added* = $C(g) \div D(g/ml) = 3,425.625 / 1.5225 =$ **2,250.0 ml**
- F. Solvent ratio (v:v) = 5% n-butanol : 95% sevoflurane = **(5/95)**
- G. *Volume of n-butanol to add* = $E(ml) \times F = 2,250.0 \times (5/95) =$ **118.42 ml**
- H. Total volume of Delipidation Solvent = E + G (ml) = 2,368.42 ml
- I. Final weight of Delipidation Solvent and Biotainer (including cap) = 3,767.909 g
- J. Final weight of Delipidation Solvent = I (g) – A (g) = 3,521.309 g
- K. **Final check – S.G. of Delipidation Solvent = $J(g) \div H(ml) = 1.4868$ g/mL**
- L. Within acceptable Range 1.4832 - 1.4903 g/mL **Yes** No (circle one)
- M. Finish: Mix Date 02/ Dec / 2009 Mix Time 06:42 **(AM/PM)** (circle one)
- N. Add 36 hours: Expiry Date: 03/ Dec / 2009 Expiry Time 6:42 /AM**(PM)** (circle one)
- O. Complete and sign Labeling Set, and attach one label to Solvent-In Bag AB (init)
- P. Attach other label to reverse side of this batch record AB (init)

MANUFACTURER:

HDL Therapeutics, Inc.
601 21st Street, Suite 300
Vero Beach, FL 32960 USA

Humanitarian Device

Authorized by Federal law for use to reduce coronary atheroma in adult patients with homozygous familial hypercholesterolemia (HoFH) who are either inadequately responsive or intolerant of maximal therapy for HoFH. The effectiveness of this device for this use has not been demonstrated.

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