LIFE 21® apheresis unit
Therapeutic Plasma Exchange (TPE)

User Manual

Software version 7.2 or higher



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LIFE 21® apheresis unit

Therapeutic Plasma Exchange (TPE)

User Manual

Software version 7.2 or higher

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Essential information

This user manual provides information, warnings and precautions for the treatment procedure Therapeutic Plasma Exchange (TPE) on the LIFE 21 apheresis unit. For further details on the device, general instructions and troubleshooting refer to the appropriate LIFE 21 apheresis unit user manuals.

NOTICE

The LIFE 21 apheresis unit with the TPE procedure is intended for professional users in health care settings and should only be used by persons that have been trained by Miltenyi Biotec authorized personnel.

IMPORTANT

Before use of the LIFE 21 apheresis unit and the respective treatments read the LIFE 21 apheresis unit user manuals carefully. Pay special attention to warnings and other information displayed on the housing of the LIFE 21 apheresis unit. Retain the LIFE 21 apheresis unit user manuals and any other safety and operating instructions provided with the products in a place accessible to all users for future reference. Disregard of any warning message can create unsafe system operations and endanger the patient, the operator, and others. Disregard of any warning messages excludes the manufacturer from any liability.

Failure to read and follow these guidelines could lead to improper or incorrect use, handling, or care of the LIFE 21 apheresis unit and could cause harm to patients and operators due to unpredictable results, device malfunction or damage, premature wear, and reduced life time of the device and may void the manufacturer's warranty.

If you are concerned about the safe use of the device or require any information about the LIFE 21 apheresis unit with the TPE procedure and its components, contact your authorized local Miltenyi Biotec service provider or call Miltenyi Biotec Technical Support.

IMPORTANT

Before using the LIFE 21 apheresis unit with the TPE procedure and its components for clinical treatments outside the European Economic Community, the regulatory approval of the LIFE 21 apheresis unit with the TPE procedure and its components in your country must be confirmed.

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1 Introduction

1.1 General information

This LIFE 21 apheresis unit user manual "Therapeutic plasma exchange (TPE)" provides information, warnings, precautions, and instructions for the operation of the LIFE 21 apheresis unit with the TPE procedure and its components. For details on device instructions, as well as general instructions and troubleshooting refer to the appropriate LIFE 21 apheresis unit user manuals provided by the manufacturer.

1.2 Process

The TPE procedure unspecifically removes pathogenic substances from the patient's plasma such as paraproteins, autoantibodies, immune complexes, protein-bound toxins, inflammatory proteins, and other plasma mediators. During a TPE procedure the disk separator as part of the tubing set separates the plasma from cellular blood components. The plasma will then be removed and replaced by defined substitution solutions. The plasma substitution solutions and the cellular blood components are given back to the patient via the blood return line (figure 1.1). During a treatment session, approximately 1–1.5 times the patient's plasma volume is exchanged.

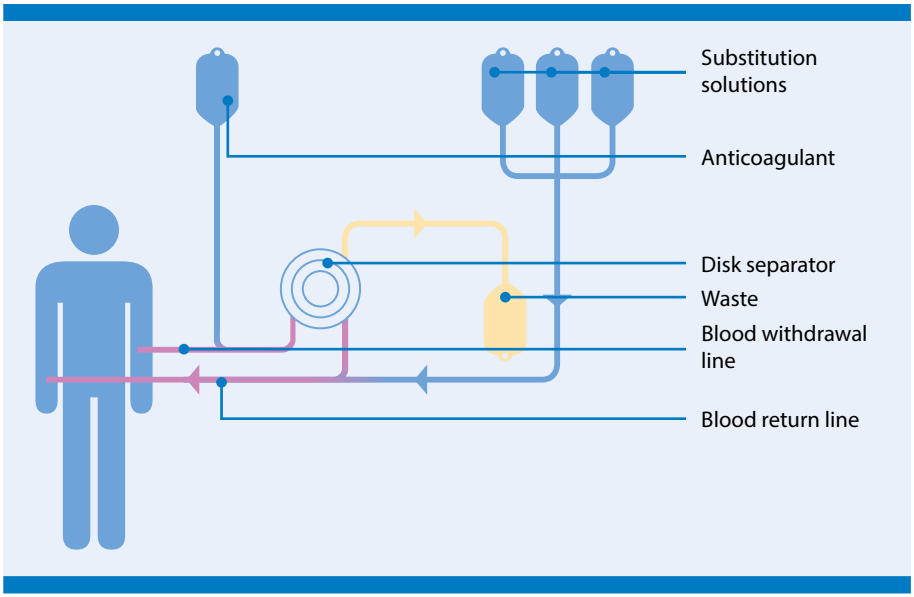


Figure 1.1: Schematic view of the TPE treatment

2
Glossary

2.1 Graphical symbols

The following chart depicts the symbols used in this user manual to inform the operator about potential risks if the outlined warnings and precautions are not followed. The hazard level classifies the hazard, as described below. The level, type, and source of the hazard, as well as potential consequences, restrictions, and measures are indicated as follows.

⚠ WARNING

Indicates a hazardous situation that, if not avoided, could result in death or serious injury.

⚠ CAUTION

Indicates a hazardous situation that, if not avoided, could result in minor or moderate injury.

NOTICE

Indicates information considered important, but not hazard-related (e.g. messages relating to property damage).

IMPORTANT

Advises the user of important practices or information not related to personal injury nor property damage.

2.2 Glossary of symbols

Refer to the LIFE 21 apheresis unit user manual “Device instructions” for more details on symbols displayed on the device. Generally applicable symbols and terms can be found in the LIFE 21 apheresis unit user manual “General instructions and troubleshooting”.

3
Materials required

3.1 LIFE 21 apheresis unit – treatment components

The following materials are required for the LIFE 21 apheresis unit with the TPE procedure (Table 3.1).

Material	Quantity	Catalogue number
LIFE 21 apheresis unit (Software version 7.0 or higher)	1	330-000-621/ 330-000-622
Patient chip card (PCC)	1	330-000-131
TheraSorb - TS TPE	1	330-000-623

Table 3.1: Materials needed for TPE procedure

⚠ WARNING

Use only the materials listed above. Miltenyi Biotec is not liable for the use of unauthorized material.

3.2 Additional materials

Besides the components described above, additional materials are required for the LIFE 21 apheresis unit with the TPE procedure (Table 3.2).

Material	Amount recommended
0.9% sodium chloride solution, for infusion, spike port	min. 500 mL for priming, higher volumes needed if used for dilution of solutions or as substitution solution
Heparin, anticoagulant solution or equivalent	5000 IU/mL, 5 mL solution
Substitution solutions (e.g. human albumin) for infusion, spike port or female Luer Lock	Defined by the treating physician
Venous access (16 G needle, or equivalent)	1 or 2
(optional) Blood warmer (ASTOTHERM® PLUS, or equivalent)	1
(optional) Blood warmer extension line (ASTOTUBE®, or equivalent)	1

Table 3.2: Additional materials needed for TPE procedure

IMPORTANT

The treatment requires the use of components that are not part of LIFE 21 apheresis unit. Use only materials and solutions that are certified for medical use in the country of the user.

4

Warnings and precautions

4.1 General warnings and precautions

Warnings and precautions regarding the LIFE 21 apheresis unit can be found in the LIFE 21 apheresis unit user manual “Device instructions”. Generally applicable warnings and precautions can be found in the LIFE 21 apheresis unit user manual “General instructions and troubleshooting”.

⚠ WARNING

Read, study, understand, and follow all safety information, warnings, precautions, and instructions provided by Miltenyi Biotec before using the LIFE 21 apheresis unit with the TPE procedure. Do not use or attempt to use the device unless an authorized Miltenyi Biotec instructor has trained you.

IMPORTANT

Any serious incident that has occurred in relation to this product should be reported to Miltenyi Biotec B.V. & Co. KG – using the contact information provided – and the competent authority of the member state in which the user of this product is established and in which the patient has been treated.

4.2 TPE procedure

4.2.1 Intended use

The LIFE 21 apheresis unit with the TPE procedure is intended for the exchange of a pre-defined volume of patient plasma against a pre-defined combination of substitution solutions. TPE is a nonspecific and nonselective therapy for the removal of pathogenic substances from the plasma.

4.2.2 Areas of application

The American Society for Apheresis (ASFA) is charged with reviewing, updating and categorizing indications for the evidence-based use of therapeutic apheresis (TA) in human disease. The latest edition (2019) lists indications for the use of therapeutic plasma exchange with 3 different grades of recommendation (categories).

Category I comprises disorders, for which plasma exchange is accepted as first-line therapy, either as a primary standalone treatment or in conjunction with other modes of treatment.

Disease	Indication
Acute inflammatory demyelinating polyradiculoneuropathy (Guillain-Barré syndrome)	Primary treatment
Anti-glomerular basement membrane disease (Goodpasture syndrome)	Diffuse alveolar hemorrhage (DAH) Dialysis-independence
Catastrophic antiphospholipid syndrome (CAPS)	
Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)	
Focal segmental glomerulosclerosis (FSGS)	Recurrent in kidney transplant
Hyperviscosity in hypergammaglobulinemia	Symptomatic Prophylaxis for rituximab
Myasthenia gravis	Acute, short-term treatment
N-methyl-D-aspartate receptor antibody encephalitis	
Paraproteinemic demyelinating neuropathies; Chronic acquired demyelinating polyneuropathies	IgG/IgA/IgM
Thrombotic microangiopathy, complement mediated	Factor H autoantibody

Disease	Indication
Thrombotic microangiopathy, drug associated	Ticlopidine
Thrombotic microangiopathy, thrombotic thrombocytopenic purpura (TTP)	
Transplantation, liver	Desensitization, ABOi living donor
Transplantation, renal, ABO compatible	Antibody mediated rejection Desensitization, living donor
Transplantation, renal, ABO incompatible	Desensitization, living donor
Vasculitis, ANCA-associated (AAV)	MPA/GPA/RLV: RPGN, Cr ≥ 5.7 MPA/GPA/RLV: DAH
Wilson disease, fulminant	

Table 4.1: Diseases with catergory I recommendation by ASFA

Category II comprises disorders for which plasma exchange is accepted as second-line therapy, either as a standalone treatment or in conjunction with other modes of treatment.

Disease	Indication
Acute disseminated encephalomyelitis (ADEM)	Steroid Refractory
Autoimmune hemolytic anemia, severe	Severe cold agglutinin disease
Cryoglobulinemia	Severe/symptomatic
Familial hypercholesterolemia	Homozygotes/Heterozygotes
Lambert-Eaton myasthenic syndrome	
Multiple sclerosis	Acute attack/relapse
Myasthenia gravis	Long-term treatment
Myeloma cast nephropathy	
Neuromyelitis optica spectrum disorders (NMOSD)	Acute attack/relapse
Overdose, envenomation, and poisoning	Mushroom poisoning
Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS); Sydenham's chorea	PANDAS, exacerbation
Phytanic acid storage disease (Refsum's Disease)	
Steroid-responsive encephalopathy associated with autoimmune thyroiditis (Hashimoto's encephalopathy)	
Systemic lupus erythematosus (SLE)	Severe complications

Disease	Indication
Thyroid storm	
Transplantation, cardiac	Desensitization
Transplantation, hematopoietic stem cell, ABO incompatible (ABOi)	Major ABOi HPC(M) Major ABOi HPC(A)
Transplantation, renal, ABO incompatible	Antibody mediated rejection
Vasculitis, other	Hepatitis B polyarteritis nodosa
Voltage-gated potassium channel (VGKC) antibody related diseases	

Table 4.2: Diseases with catergory II recommendation by ASFA

Category III comprises disorders, in which the optimum role of plasma exchange is not established. Decision making should be individualized.

Disease	Indication
Acute liver failure	
Anti-glomerular basement membrane disease (Goodpasture syndrome)	Dialysis-dependence, no DAH
Atopic (neuro-) dermatitis (atopic eczema), recalcitrant	
Autoimmune hemolytic anemia, severe	Severe warm autoimmune
Burn shock resuscitation	
Cardiac neonatal lupus	
Chronic focal encephalitis (Rasmussen Encephalitis)	
Coagulation factor inhibitors	
Complex regional pain syndrome	Chronic
Dilated cardiomyopathy, idiopathic	NYHA II-IV
Erythropoietic protoporphyria, liver disease	
Focal segmental glomerulosclerosis (FSGS)	Steroid resistant in native kidney
Hemolysis, elevated liver enzymes, and low platelets syndrome (HELLP Syndrome)	Postpartum
Hemophagocytic lymphohistiocytosis (HLH); Hemophagocytic syndrome; Macrophage activating syndrome	
Heparin-induced thrombocytopenia and thrombosis (HIT/HITT)	Pre-cardiopulmonary bypass Thrombosis
Hypertriglyceridemic pancreatitis	Severe Prevention of relapse
IgA nephropathy (Berger's Disease)	Crescentic Chronic progressive
Immune thrombocytopenia (ITP)	Refractory

Disease	Indication
Multiple sclerosis	Chronic
Nephrogenic systemic fibrosis	
Neuromyelitis optica spectrum disorders (NMOSD)	Maintenance
Overdose, envenomation, and poisoning	Envenomation Drug overdose/poisoning
Paraneoplastic neurological syndromes	
Paraproteinemic demyelinating neuropathies; Chronic acquired demyelinating polyneuropathies	Anti-MAG neuropathy Multiple myeloma
Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS); Sydenham's chorea	Sydenham's chorea, severe
Pemphigus vulgaris	Severe
Post-transfusion purpura (PTP)	
Progressive multifocal leukoencephalopathy (PML) associated with natalizumab	
Pruritus due to hepatobiliary diseases	Treatment resistant
Red cell alloimmunization, prevention and treatment	Pregnancy, GA < 20 wks
Scleroderma (Systemic sclerosis)	
Sepsis with multiorgan failure	
Stiff-person syndrome	
Sudden sensorineural hearing loss	
Thrombotic microangiopathy, complement mediated	Complement factor gene mutations
Thrombotic microangiopathy, drug associated	Clopidogrel
Thrombotic microangiopathy, infection associated	STEC-HUS, severe pHUS
Thrombotic microangiopathy, transplantation associated	
Toxic epidermal necrolysis (TEN)	Refractory
Transplantation, cardiac	Antibody mediated rejection
Transplantation, hematopoietic stem cell, ABO incompatible (ABOi)	Major/Minor ABOi w/ pure RBC aplasia
Transplantation, hematopoietic stem cell, HLA desensitization	

Disease	Indication
Transplantation, liver	Desensitization, ABOi deceased donor/ Antibody mediated rejection
Transplantation, lung	Antibody mediated rejection/ desensitization
Transplantation, renal, ABO compatible	Desensitization, deceased donor
Vasculitis, ANCA-associated (AAV)	MPA/GPA/RLV: RPGN, Cr < 5.7 EGPA
Vasculitis, IgA (Henoch-Schönlein purpura)	Crescentic RPGN Severe extrarenal manifestations
Vasculitis, other	Behcet's disease

Table 4.3: Diseases with catergory III recommendation by ASFA

4.2.3 Contra indications of therapeutic plasma exchange

- Clinical conditions that prohibit transitory volume changes or loss of plasma constituents
- Indications that prohibit anticoagulation using Heparin and/or ACD-A solutions
- Hypercoagulability
- Generalized viral, bacterial and/or mycotic infections
- Severe immune deficiencies (e.g. AIDS)
- IgA deficiency

4.2.4 Side effects

General

According to the data of the World Apheresis Association (WAA) apheresis registry (Mörtzell Henriksson et al. Transfusion Apher Sci 54:2;2016), adverse events of therapeutic apheresis in general were registered as mild in 2.9%, as moderate in 6.6%, and severe in 1.0% of treatments. The only severe adverse event (interruption of treatment) with an occurrence of more than 10 per 10,000 procedures was hypotension/syncope. Severe adverse events with an occurrence of 1–10 cases per 10,000 were urticaria, fever/chills, nausea/vomiting, access problems, flush, tingling/stitching, arrhythmia, bronchospasm, Quincke edema. The most common moderate adverse events (need of medication) with an occurrence of more than 10 per 10,000 procedures were tingling, urticaria, and hypotension. The most common mild adverse events (tolerated without

medication) with an occurrence of more than 10 per 10,000 procedures were access problems, hypotension, tingling, device problems, urticaria, nausea/vomiting, and hematoma at puncture site.

Activation and elimination of thrombocytes is possible due to the elements of plasma separation in the therapy. A decrease in platelet count of app. 15% is commonly observed during apheretic procedures. Therefore, blood control measures before and after the therapy is recommended.

Heparin-induced thrombocytopenia and hemolysis can occur when heparin is solely used as an anticoagulant.

For patients with progressive heart diseases, extracorporeal therapies may lead to an increase in angina pectoris or dyspnea due to the extracorporeal blood volume necessary for the therapy.

An increase in the pH of the blood within the normal range or metabolic alkalosis can occur with the use of citrate as anticoagulant. If hepatic citrate metabolism is impaired the use of citrate as anticoagulant may result in metabolic acidosis.

Enhanced drop in blood pressure may occur when treating patients under ACE-inhibitor medication.

In patients with a central venous access, cases of central line thromboses and catheter associated infections were described.

Plasma exchange related side effects

Adverse events of therapeutic plasma exchange using filtration technology were registered in the WAA registry as mild in 2.9%, as moderate in 6.6%, and severe in 1.0% of treatments.The occurrence of side effects depends on the substitution solution used. Albumin (3.5%–5% end concentration) induces 0.2–1.3% mild, 2.9–3.6% moderate, and 0.6–0.7% severe side effects. The rates for liquid stores plasma are higher with 2.4% mild, 5.9% moderate, and 1.3% severe side effects. Fresh frozen plasma induces 1.3% mild, 6.0% moderate, and 0.7% severe side effects. Hydroxy ethyl starch and other replacement solutions show a lower rate of side effects.

Following the infusion of plasma or human albumin as replacement, the most common severe side effects with an occurrence of more than 10 per 10,000 are urticaria/conjunctivitis, chills/fever, and hypotension/syncope. Moderate side effects with an occurrence of more than 10 per 10,000 treatments are urticaria/conjunctivitis, tingling/stitching, hypotension, chills/fever, flush, and hypertension. Except for hypotension, all side effects mentioned are more common when plasma is given as replacement solution.

The risk of hypotensive reaction is increased when using partial saline replacement (80% albumin, 20% saline) compared to pure albumin replacement (Irani, 2019).

The transmission of infectious agents can not completely be excluded if preparations of donor plasma are used as replacement solution.

During a single treatment with TPE, using replacement solutions other than plasma, the activity of coagulation factors decreases. There are significant reductions in fibrinogen, FV, FVII, FVIII, FIX, FX, and von Willebrand Factor (up to 70% for 1.2 treated plasma volumes).
Therapeutic plasma exchange removes medications from the blood, mainly Diclofenac, Chloramphenicol, IFN-alpha, Tobramycin, Ceftriaxone, Cisplatin, Vincristine, Verapamil, Ceftazidime, Diltiazem, Propoxyphene, Propranolol, and others. Side effects due to the removal of those drugs have to be taken into consideration.

Increased rate of infections, if immunoglobulin-free replacement solutions are used, particularly in patients, who are immunocompromized and who receive immunosuppressive drugs.

⚠ WARNING

Some severe cases of anaphylactic shock are due to an interaction between infused IgA and class-specific anti-IgA in the recipient's plasma but in many cases the cause of the reaction is unknown. In case of anaphylactic reactions, the infusion of plasma must be immediately interrupted and anti-allergic drugs administered.

4.2.5 Precautions

Use of electrolyte solution for substitution should be strictly limited in case of hypoproteinemia, edema, or coagulation disorders. Fresh frozen plasma (FFP) usually contains citric acid for anticoagulation. The application of FFP should therefore be accompanied by careful monitoring of plasma calcium levels and administration of calcium if clinical symptoms occur. More information is given in the chapter "Anticoagulation" in the user manual "General instructions and troubleshooting".

5
Warnings and precautions

The TPE procedure on the LIFE 21 apheresis unit is fully automated and requires only a few preparative steps.

⚠ CAUTION

Observe adequate hygienic measures for aseptic handling for all preparative steps.

5.1 Preparation of solutions

It is recommended to bring all solutions to ambient temperature well tolerated by the patient, and/or to connect a blood warmer to the tubing set (refer to chapter 6.4.1). If a blood warmer is needed later on during the treatment, refer to chapter 7.3.8.

5.2 Anticoagulation

In order to prevent blood or plasma coagulation in the extracorporeal circuit during the treatment process, the blood must be anticoagulated. Anticoagulation should be individually adapted for each patient in accordance with the instructions given by the attending physician.

Refer to the LIFE 21 apheresis unit user manual “General instructions and troubleshooting” for the recommended combination of the anticoagulation solutions ACD-A and Heparin. Recommendations regarding calcium substitution can also be found in the LIFE 21 apheresis unit user manual “General instructions and troubleshooting”.

6

Set-up of the LIFE 21 apheresis unit

The following chapter describes step-by-step how to set-up the LIFE 21 apheresis unit for the TPE procedure. The procedure is divided into the following steps:

- Initialization of the LIFE 21 apheresis unit
- Tubing set installation – Part 1
- Settings for patient and treatment parameters
- Tubing set installation – Part 2
- Automatic priming of extracorporal system
- Connection of patient (selection of single/double needle mode)

The different steps will be elucidated by displaying the appropriate software screens and by stating the specific operator action required.
The procedure described in this chapter reflects a first TPE treatment using a new patient chip card. Deviations to this process for consecutive treatment runs are indicated in *italic* characters.

6.1 Initialization process

Operator action: Switch on the LIFE 21 apheresis unit by attaching the power cable to a suitable power outlet and activating the power switch located on the back panel of the device.
After the initialization phase, the first screen is displayed showing a menu with different treatment options.

Operator action: Insert patient chip card into the chip card drive and select the TPE procedure by pressing the button **TheraSorb-TPE** (Screen 6.1).

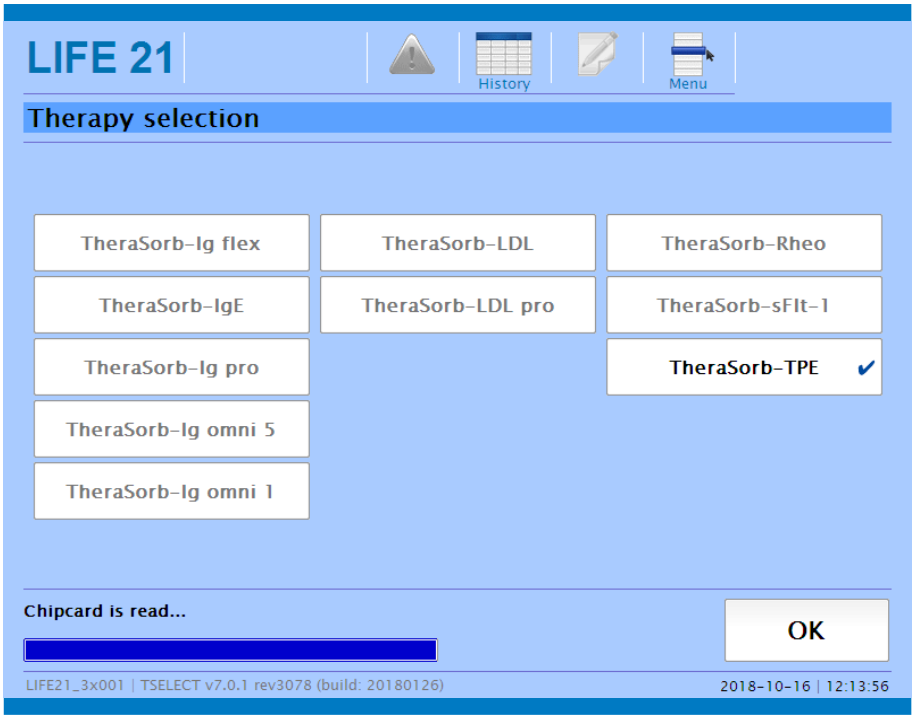
For consecutive treatments of the same patient the procedure is, after inserting the patient chip card, automatically selected based on the last treatment performed.

IMPORTANT
Make sure to insert the chip site of the card into the slot with the gold-colored chip facing towards you. Treatment related data and material information is transferred to the chip card during the process to prevent any mismatching during subsequent treatment of the patient. At the end of the process, treatment-related and patient-related information will be transferred to the chip card. After every treatment the previous information on the card will be overwritten by the current treatment-related information.

⚠ CAUTION

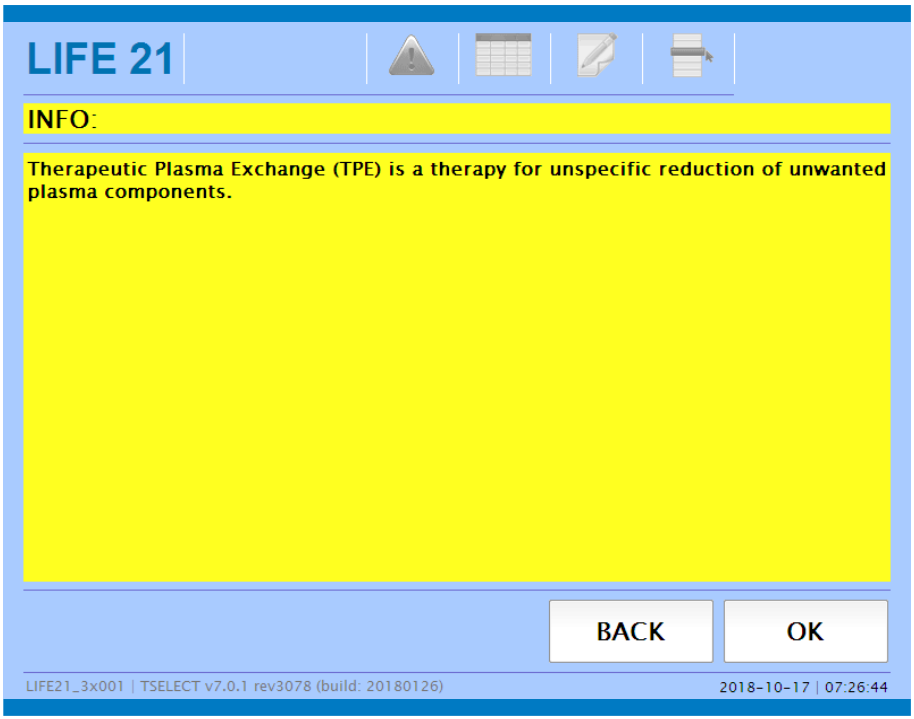
To select and to continue the process, the patient chip card is required. Do not remove the chip card unless prompted by the device. Incorrect insertion or removal may lead to data loss or data corruption. Make sure the correct patient chip card is used. To avoid any mistaken identity it is highly recommended that the patient chip card is labeled with the patient's name and date of birth before the first treatment.

IMPORTANT
A user interface showing screens with additional information, as well as requests for operator action will guide the operator through the process. For details regarding the graphical user interface, refer to the LIFE 21 apheresis unit user manual "Device instructions". The screenshots presented in this manual are representative TPE procedure screens and in some instances may differ slightly from screens displayed on the device during the treatment.



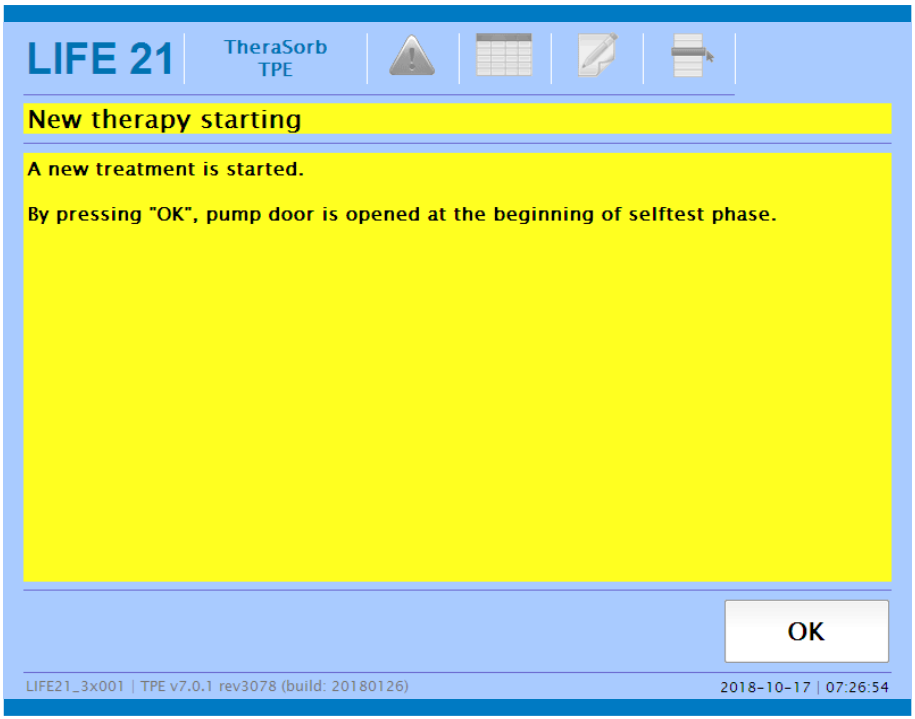
Screen 6.1: Menu with treatment options

Operator action: To proceed press **OK** after the button is activated. An information screen is displayed (Screen 6.2).



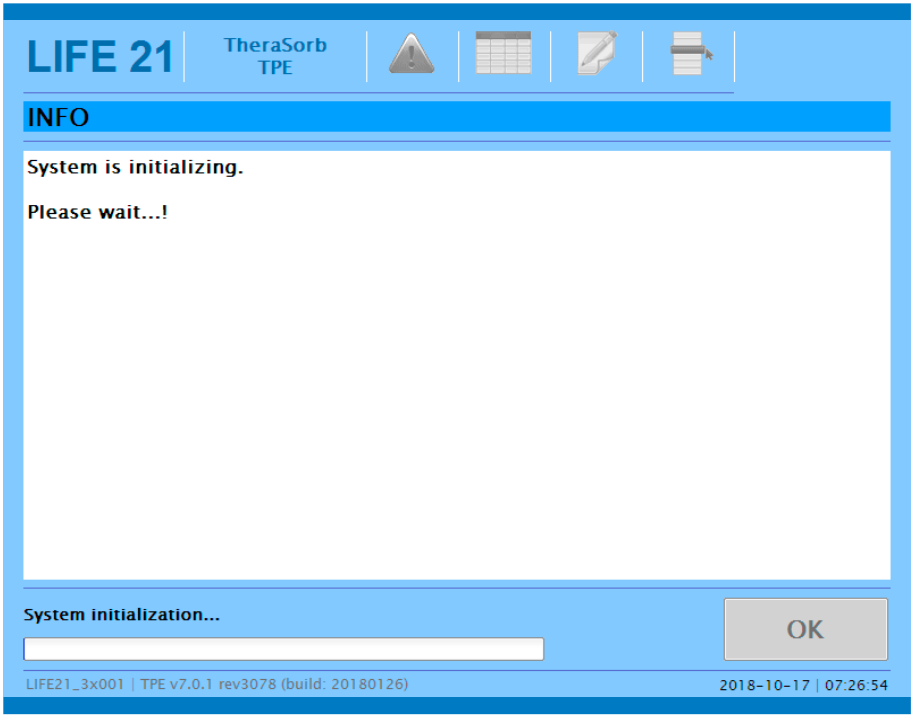
Screen 6.2: Information screen on selected therapy

Operator action: Press **OK** button in the information screen and follow the instructions on the screen (Screen 6.3). Press **OK** to proceed.



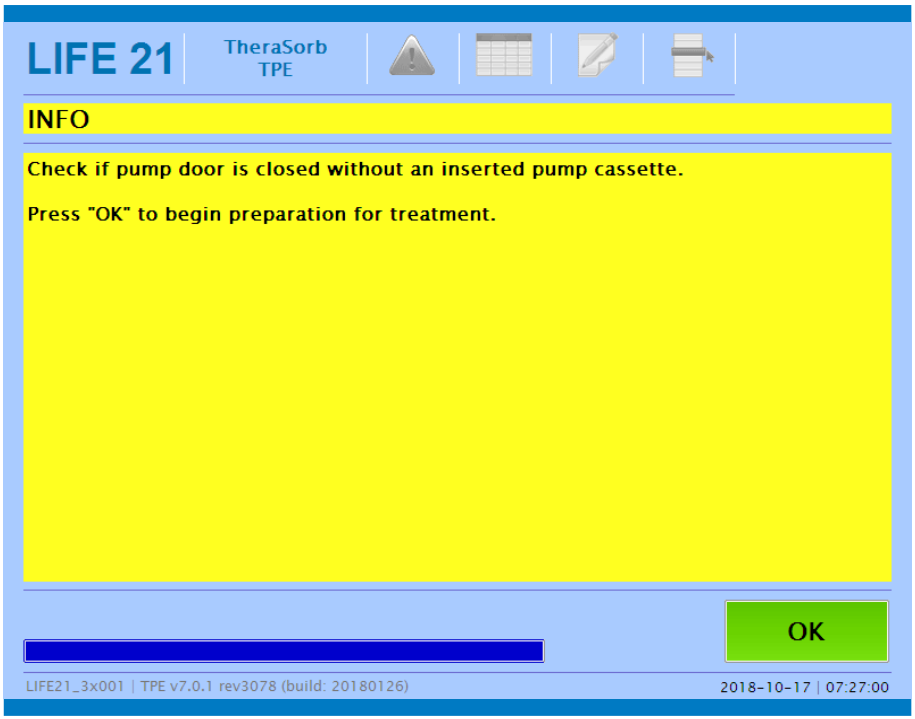
Screen 6.3: Information/status screen for self-test phase

The selected process is initialized (Screen 6.4).



Screen 6.4: Status screen with software version

Operator action: After system initialization, the next screen is displayed. Follow the instructions on the screen (Screen 6.5) and press **OK** to continue.



Screen 6.5: End of system initialization

6.2 Tubing set installation – Part 1

The following chapter guides the operator through the first part of the tubing set installation starting with an overview on the tubing set components followed by a detailed description of the installation process of the tubing set components.

6.2.1 Tubing set components and connectors

The components of the TheraSorb - TS TPE are provided in a sealed and sterilized package. The tubing set components are summarized in Figure 6.1. The TheraSorb - TS TPE represents the extracorporeal blood and fluid path during TPE procedure. It connects the patient with the anticoagulant, the substitution solutions, and delivers the plasma to the waste. It is composed of a pump cassette, a disk separator (for plasma separation), a tubing set carrier, and tubing lines with connectors to the solutions, external sensors and vascular access points of the patient.

NOTICE

Do not connect any solutions to the TheraSorb - TS TPE before the appropriate operator action is required.

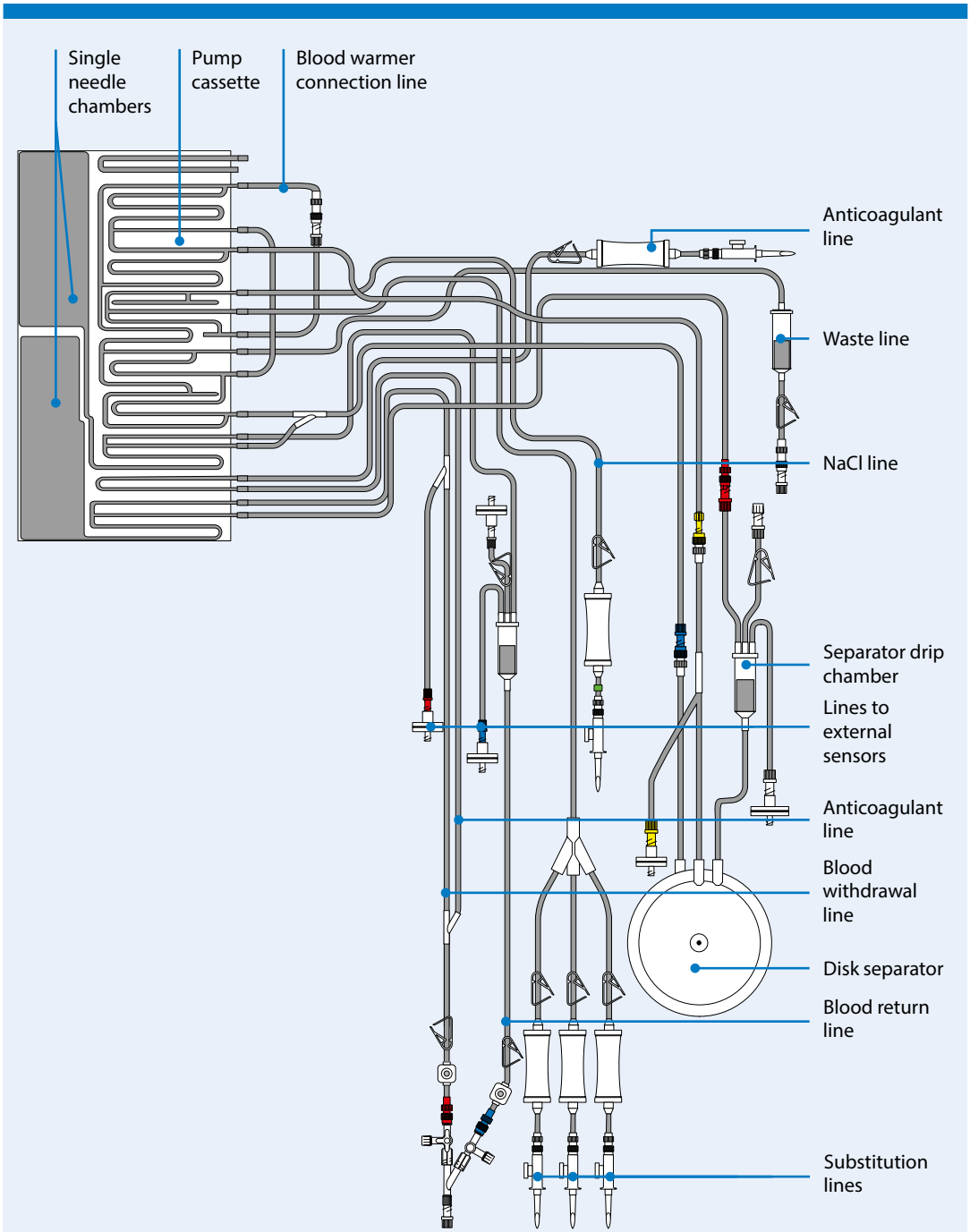


Figure 6.1: Components of the TheraSorb - TS TPE tubing set

The allocation of TheraSorb - TS TPE tubing paths, type of connectors, and color codes are summarized in Figure 6.2 and Table 6.1.

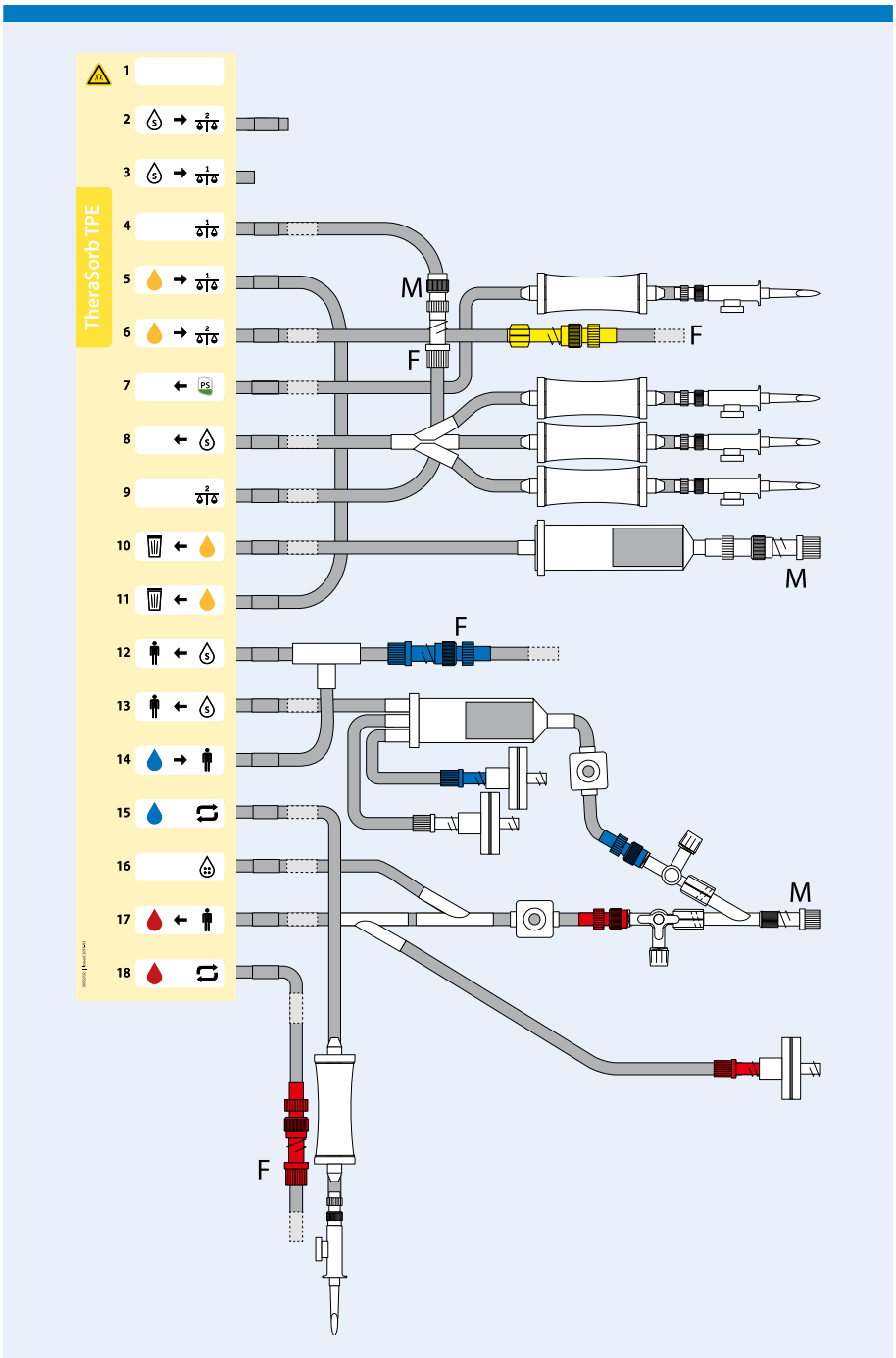
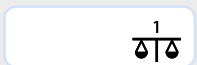
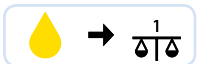
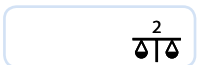


Figure 6.2: Allocation of tubing lines and connectors (M = male connector, F = female connector)

⚠ CAUTION

Observe adequate hygienic measures for aseptic handling when interconnecting tubing parts and solutions to maintain sterility of the internal fluid path.

Symbol	Explanation
	Pump 1: not used for TPE
	**Pump 2:** Substitution solution inlet 1 to balancing circuit
	**Pump 3:** Substitution solution inlet 2 to balancing circuit
	**Pump 4:** Balance pump
	**Pump 5:** Plasma inlet 1 to balancing circuit
	**Pump 6:** Plasma inlet 2 to balancing circuit
	**Pump 7:** Priming solution and NaCl substitution solution from bag to balance circuit
	**Pump 8:** Substitution solution from bag to balance circuit
	**Pump 9:** Balance pump
	**Pump 10:** Plasma from balancing circuit to waste 2
	**Pump 11:** Plasma from balancing circuit to waste 1
	**Pump 12:** Substitution solution outlet 2 from balancing circuit
	**Pump 13:** Substitution solution outlet 1 from balancing circuit
	**Pump 14:** Whole blood from blood return line to patient

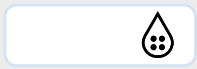
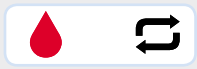
Symbol	Explanation
	**Pump 15:** Single Needle OUT chamber In/Out (in Single Needle modus only): a) Single Needle withdrawal step: Blood cell concentrate from disc separator to Single Needle OUT chamber; b) Single Needle return step: Blood cell concentrate from Single Needle OUT chamber to blood return line
	**Pump 16:** Anticoagulant from bag to blood withdrawal line
	**Pump 17:** Whole blood from blood withdrawal line to disk separator
	**Pump 18:** Single Needle IN chamber In/Out (in Single Needle modus only): a) Single Needle withdrawal step: Whole blood from blood withdrawal line to Single Needle IN chamber; b) Single Needle return step: Whole blood from Single Needle IN chamber to disk separator

Table 6.1: Explanation of symbols on the pump door label TheraSorb TPE

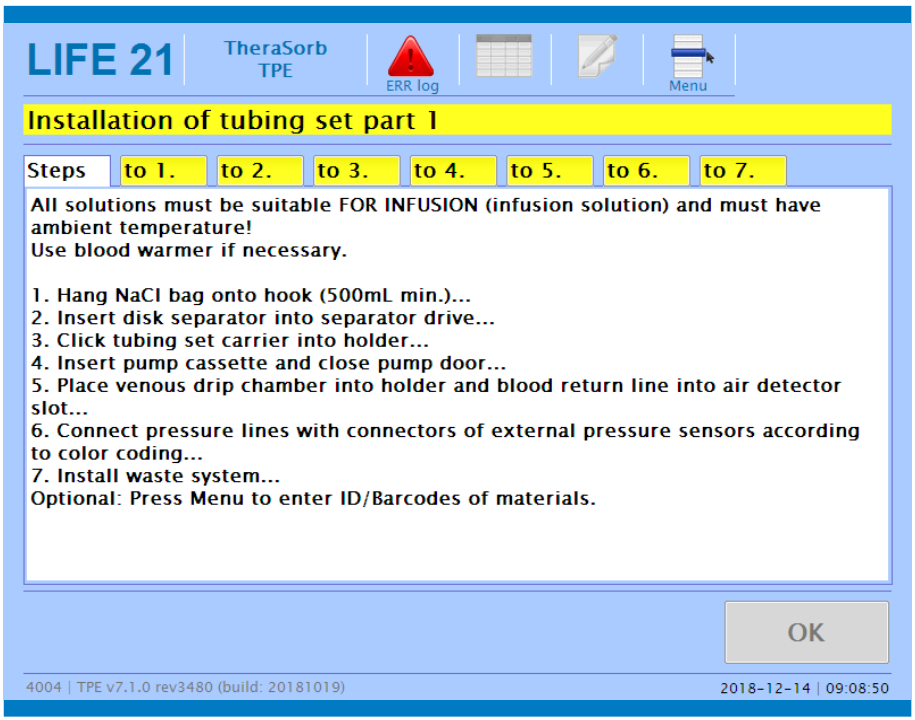
6.2.2 Installation steps

This chapter guides the operator step-by-step through the first part of the tubing set installation.

⚠ WARNING

Prior to opening the tubing set, inspect the packaging for damage, punctures, or tears. Damaged packaging could indicate that the tubing set is no longer sterile and therefore must not be used. A sterile fluid path is provided only when the packaging is intact. Luer Lock connections must be closed tightly before use.

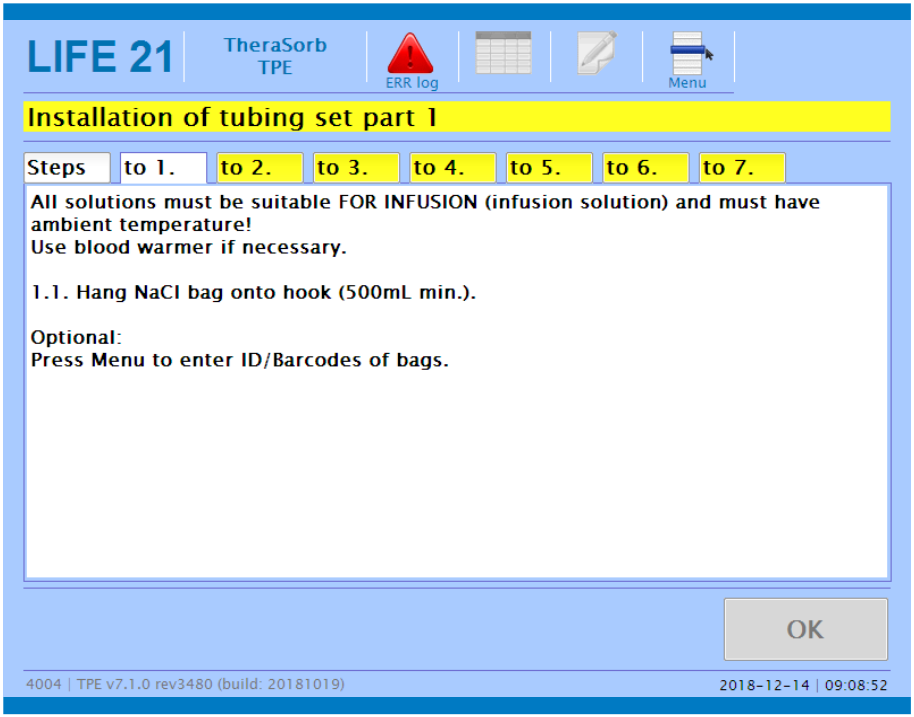
After the initialization steps are completed, the overview screen for the first part of the tubing set installation is displayed (Screen 6.6). A summary of all required steps is given under **Steps**.



Screen 6.6: Summary of all installation steps

It is highly recommended that the detailed instructions under **to 1.** through **to 7.** be followed to enable the correct installation of the tubing set.

Operator action: Press to 1. and follow the instructions on the screen (Screen 6.7).

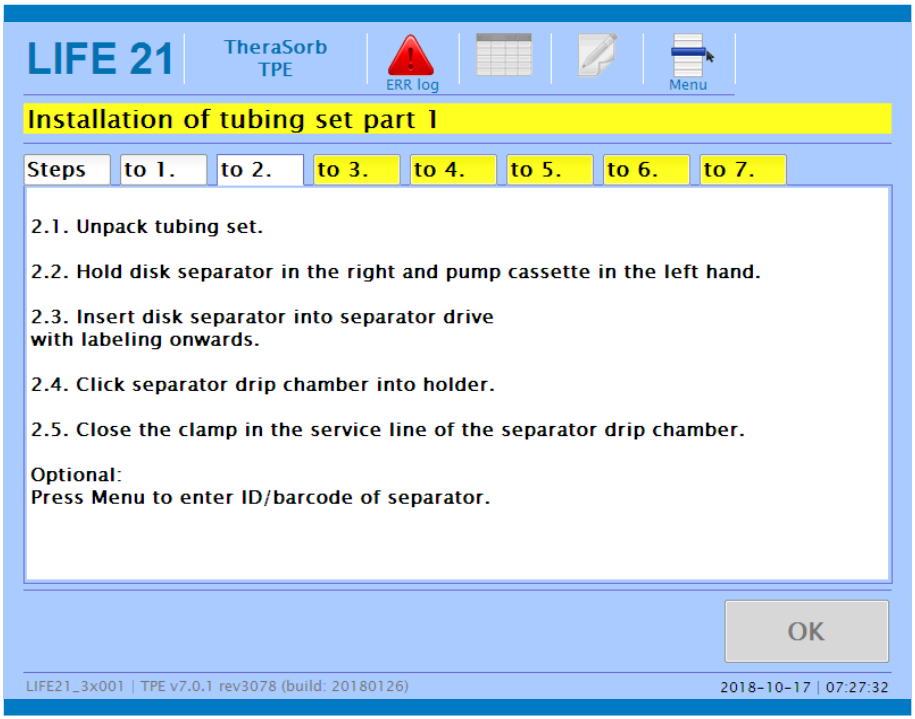


Screen 6.7: Placing solution bags on hooks

⚠ CAUTION

Make sure that the maximum load allowance of the hooks is not exceeded.

Operator action: Press **to 2.** and follow the instructions on the screen (Screen 6.8). Open tubing set package of the TheraSorb-TS TPE tubing set. Hold the disk separator in the right hand and the pump cassette in the left hand.



Screen 6.8: Installation of disk separator and separator drip chamber

⚠ CAUTION

To prevent damage to the tubing set or loss of sterility of the interior fluid path do not drop the tubing set and avoid prolonged exposure or contact of open connectors to the environment during the preparation and treatment phase!

Figure 6.3 shows the correct placement of the disk separator into the separator drive.

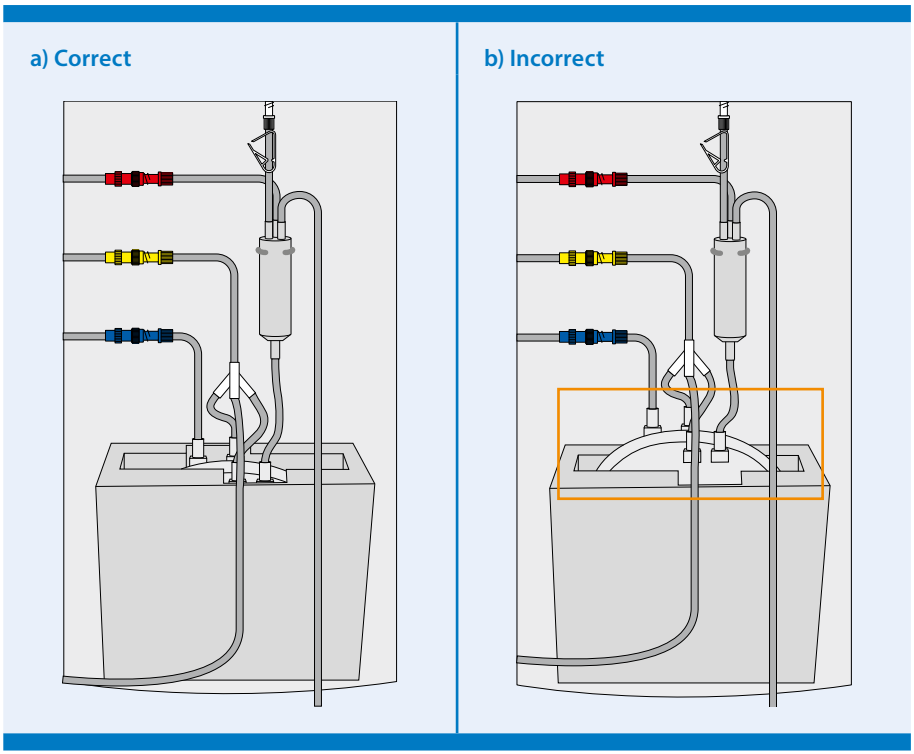
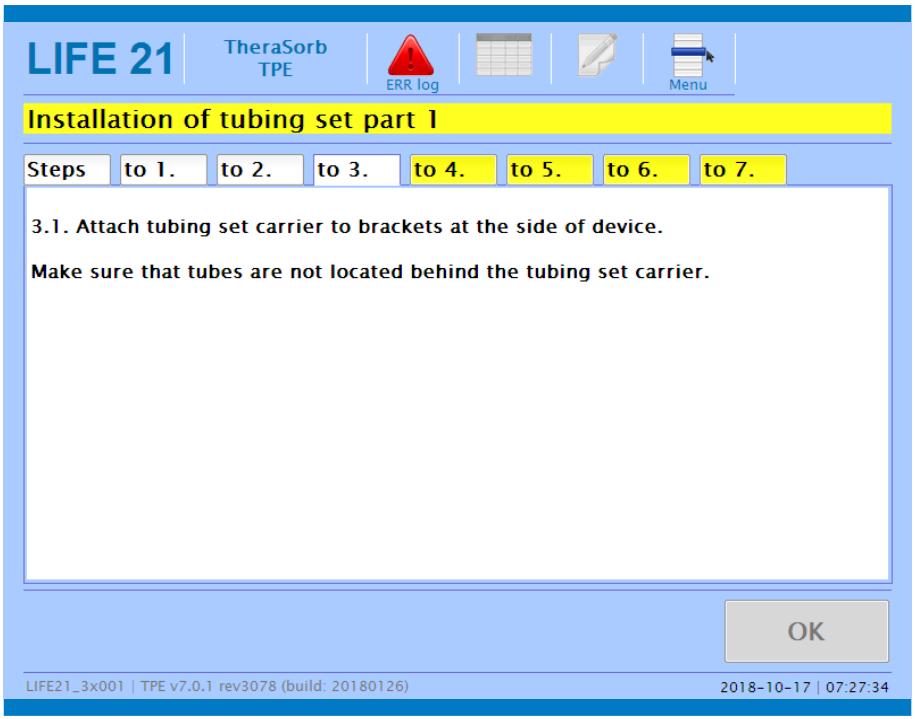


Figure 6.3: Position of disk separator in separator drive

Operator action: Press **to 3.** and follow the instructions on the screen (Screen 6.9). The correct installation of the tubing set carrier is shown in Figure 6.4.



Screen 6.9: Installation of tubing set carrier

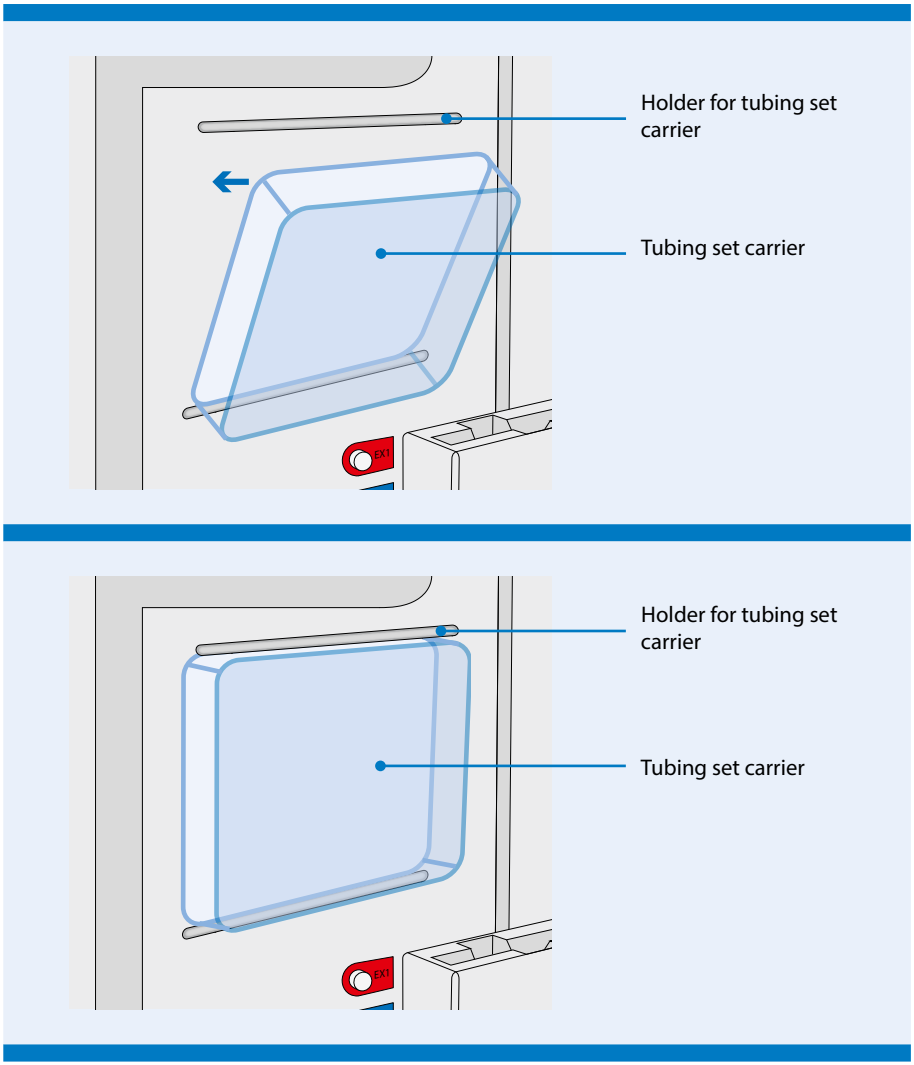
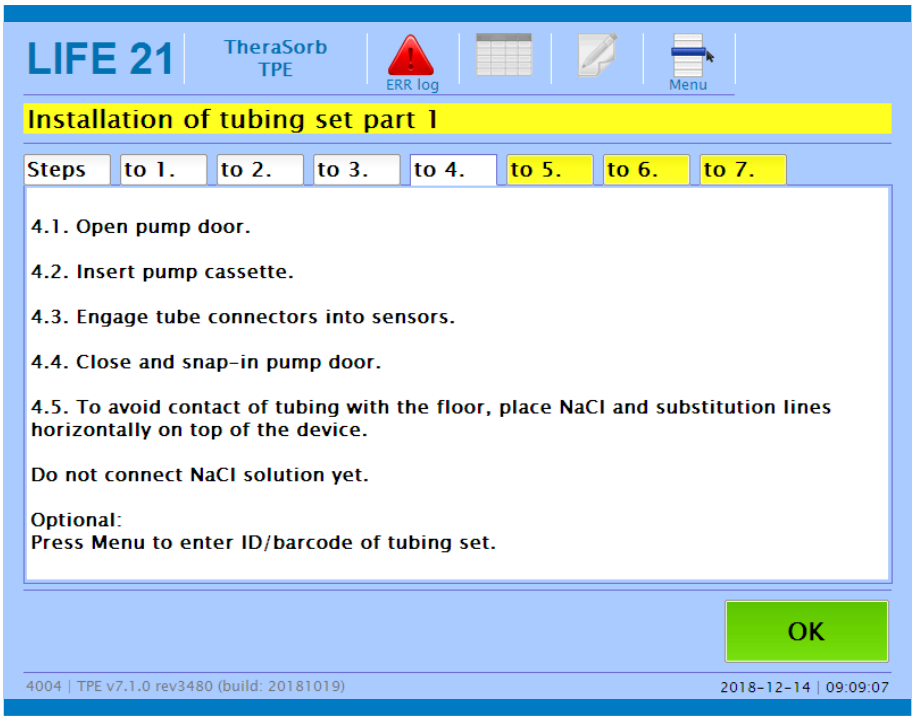


Figure 6.4: Insertion of tubing set carrier into holder (schematic view without tubing)

Operator action: Press to 4. and follow the instructions on the screen (Screen 6.10).



Screen 6.10: Installation of tubing set into pump module

Figure 6.5 shows how the pump cassette is placed into the pump module. Make sure that the tubing fits correctly into the light and pressure sensors.

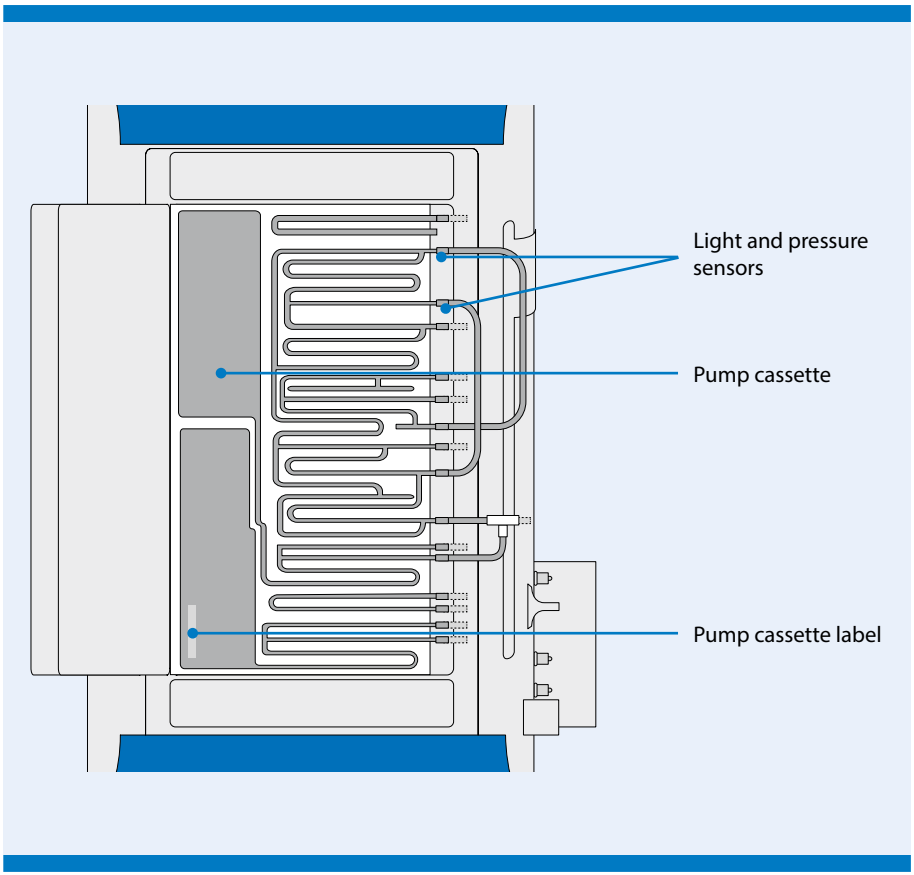
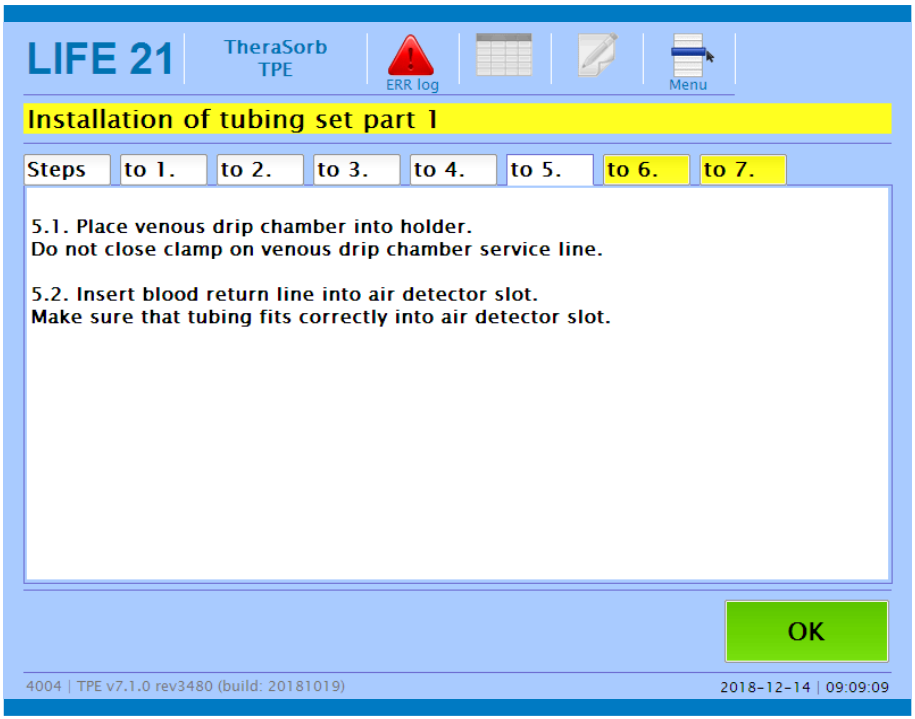


Figure 6.5: Placement of pump cassette into pump module

Operator action: Press to 5. and follow the instructions on the screen (Screen 6.11).



Screen 6.11: Installation of venous drip chamber

Figure 6.6 shows the correct position oft the venous drip chamber and the blood return line in the air detector.

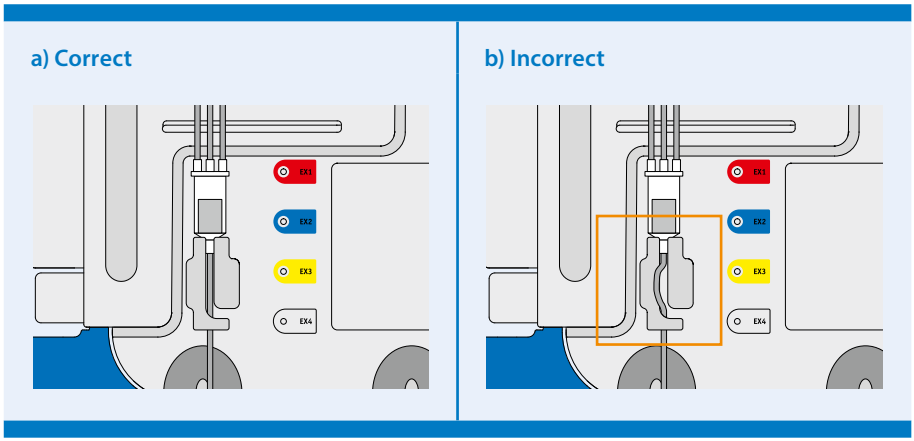
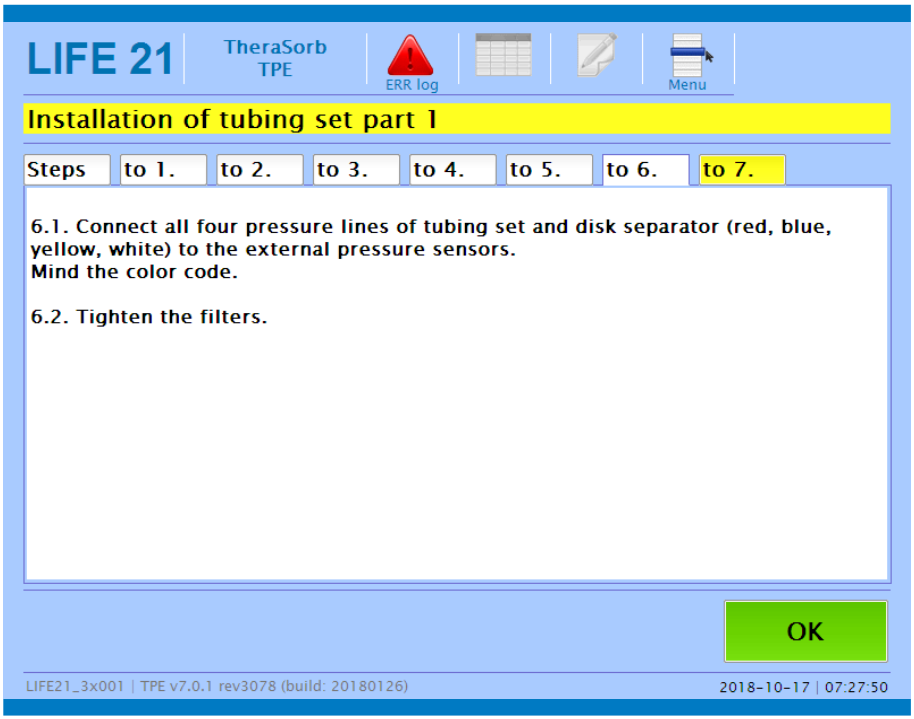


Figure 6.6: Position of venous drip chamber and blood return line

⚠ WARNING

Do not to confuse the blood return line with other lines of the tubing set when placing the tubing into the air detector. Otherwise, the returned blood cannot be monitored for the occurence of air bubbles.

Operator action: Press to 6. and follow the instructions on the screen (Screen 6.12).

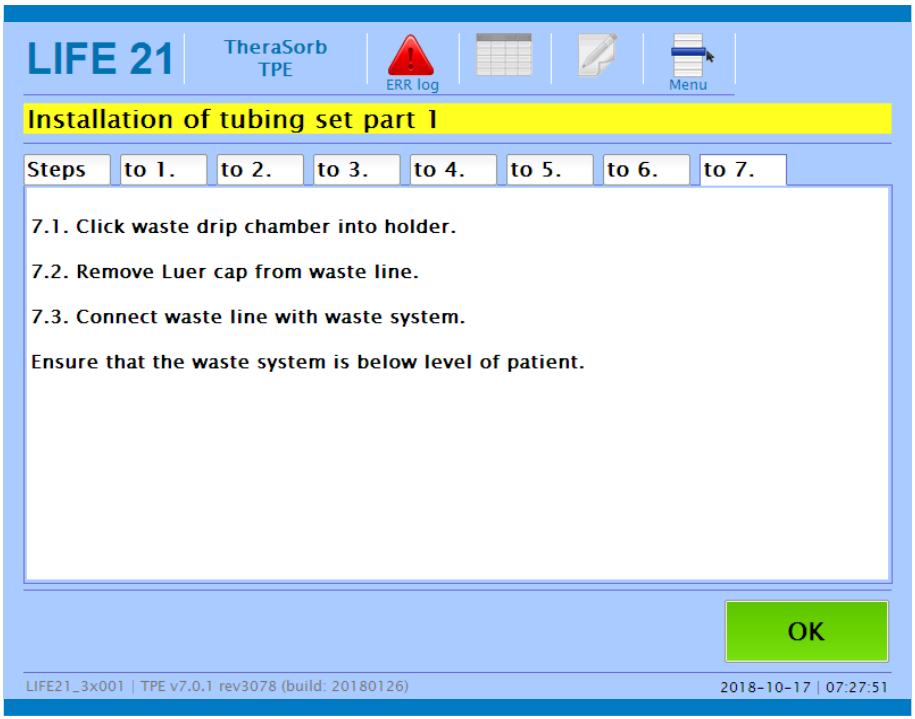


Screen 6.12: Connection of pressure lines to external sensors

NOTICE

After connecting the hydrophobic filters to the sensors make sure that all Luer Lock connections are tight. Do not overtighten the connections and avoid any kind of breaks or tears.

Operator action: Press to 7. and follow the instructions for subsection 7.1 and 7.2 on the screen (Screen 6.13).



Screen 6.13: Connection of waste line

Operator action: For subsection 7.3 on screen Screen 6.13 follow the instructions below:

- Unfold and place one waste bag onto the bag hangers located on the left side of the housing.
- Make sure that the bag is placed onto two separate hangers with one eyelet each.

⚠ CAUTION

The maximum weight of a bag hanger is limited to not more than 10 kg.

- The markers on the bag indicating the approximate fill volume must be visible to the operator.
- Check that the outlet at the bottom of the bag is completely closed to avoid spillage of the potentially infectious waste fluids.
- Connect the waste line of the TheraSorb - TS TPE tubing set (male Luer Lock connector) securely to the female Luer Lock connector of the fill tubing of the waste bag.

⚠ CAUTION

The drip chamber of the waste line has to be in an upright position and the waste bag or the connection to the central waste line should not be higher than level of patient, to avoid any retrograde contamination. If this cannot be guaranteed an independent back flow prevention must be installed.

IMPORTANT

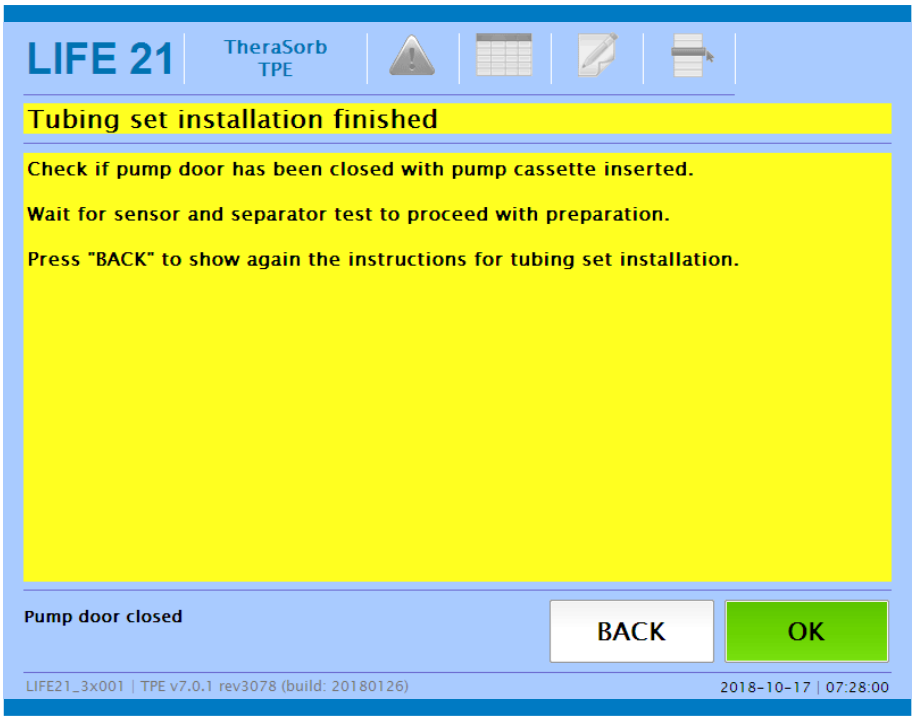
Save the cap of the fill tubing of the waste bag for later use.

- Open the clamps on the waste line and the fill tubing of the waste bag.
- Press **OK** to continue the set-up.

⚠ WARNING

Exceeding the fill volume of 10 L specified by the bag manufacturer can cause a rupture of the bag and spillage of potentially infectious material. Carefully monitor the fill level of the waste bag as indicated by the markers on the bag surface. Overfilling may also cause the bag to slip off the bag hanger or cause a breakage of the bag hanger itself. In case of spillage, observe local precautions and regulations for the handling of infectious materials.

Operator action: Follow instructions on the screen (Screen 6.14) and then press **OK**.



Screen 6.14: Finalization of tubing set installation

The device performs internal tests before the next screen is shown (Screen 6.15).

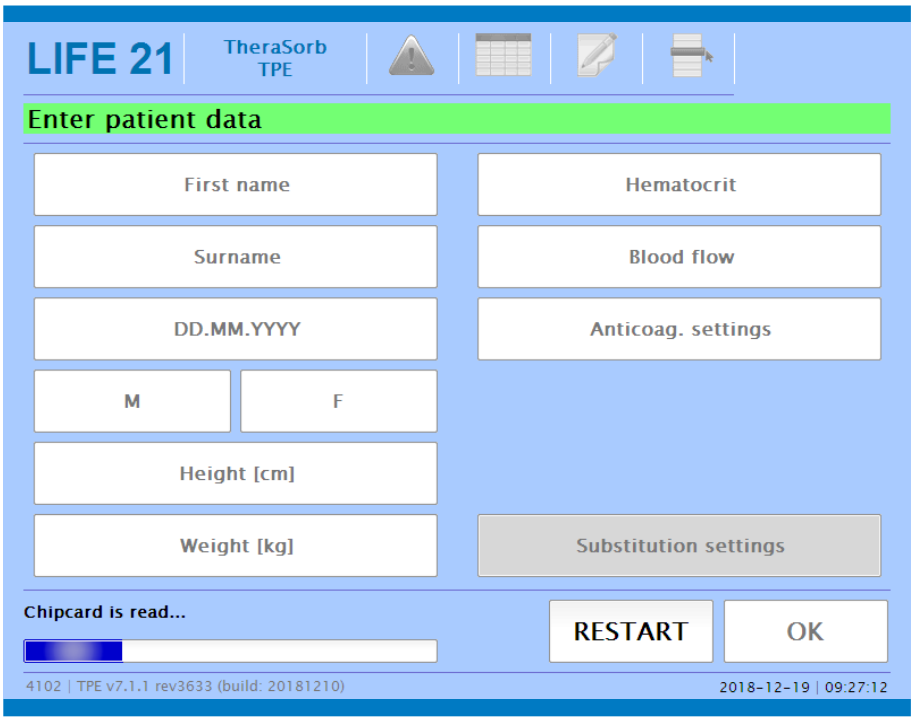
6.3 Input of patient and treatment-related settings

The following chapter guides the operator through the entry of patient and treatment-related settings. The procedure described in this chapter reflects the settings for a first TPE treatment using a new patient chip card.

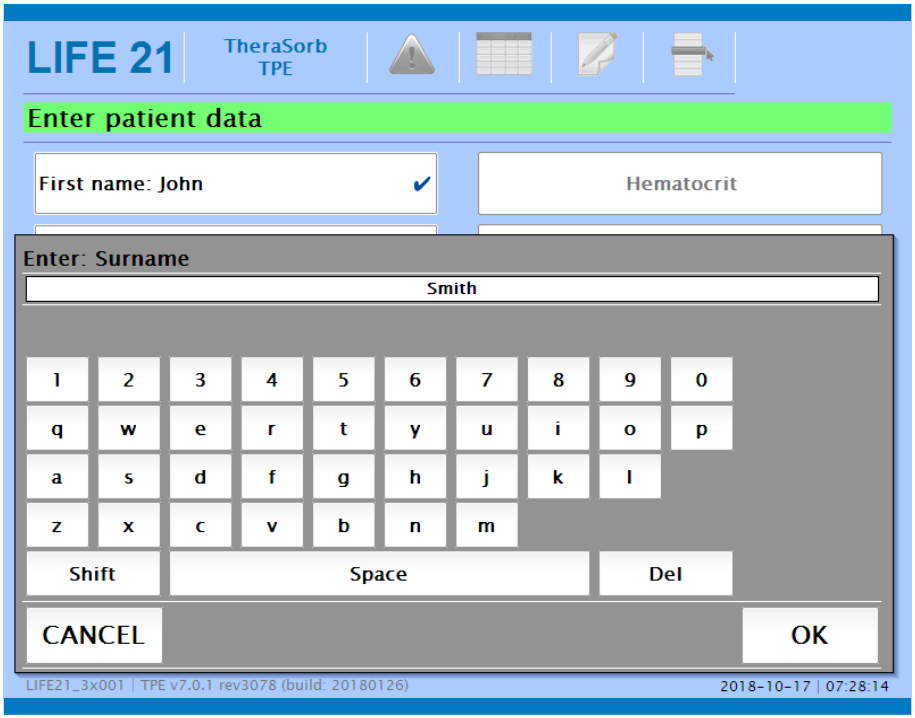
6.3.1 General parameters

Operator action: The operator needs to enter patient-related parameters (Screen 6.15). Enter the patient-related data by pressing the respective buttons on the screen as well as treatment-related settings such as blood flow and hematocrit. A data entry mask allows the operator to enter the data using a keypad, and to confirm the entry by pressing **OK** (Screen 6.16).

In case of consecutive patient treatments, parameters from the patient chip card will be displayed on the screen automatically. Missing parameters or required modifications need to be entered as described above.



Screen 6.15: Entry of patient-related data (first treatment)



Screen 6.16: Representative data entry mask with alpha-numeric keypad

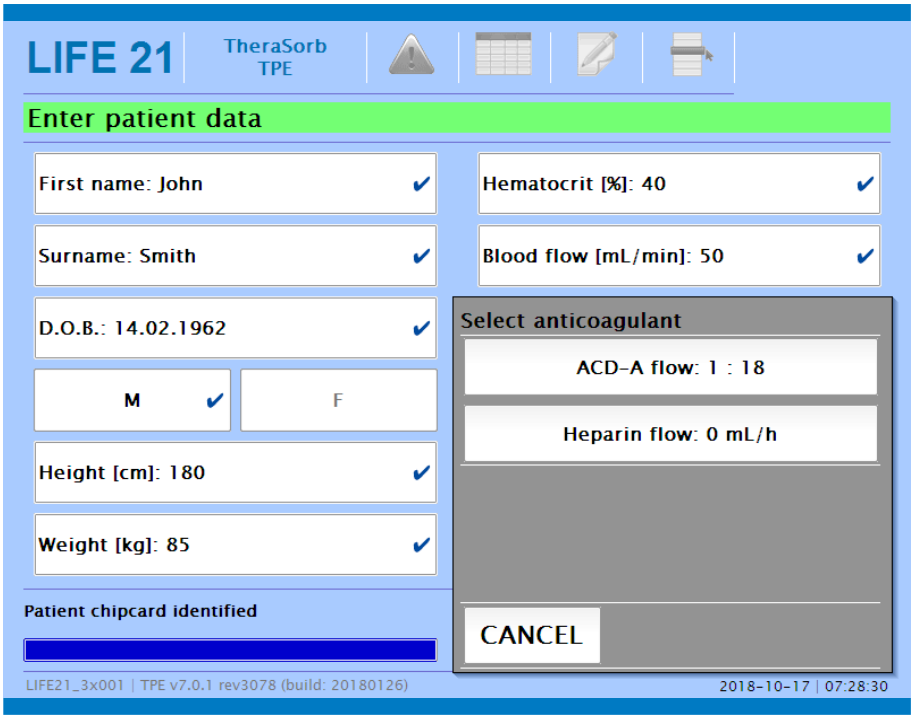
Completed fields are displayed with a check mark (tick).

6.3.2 Anticoagulation settings

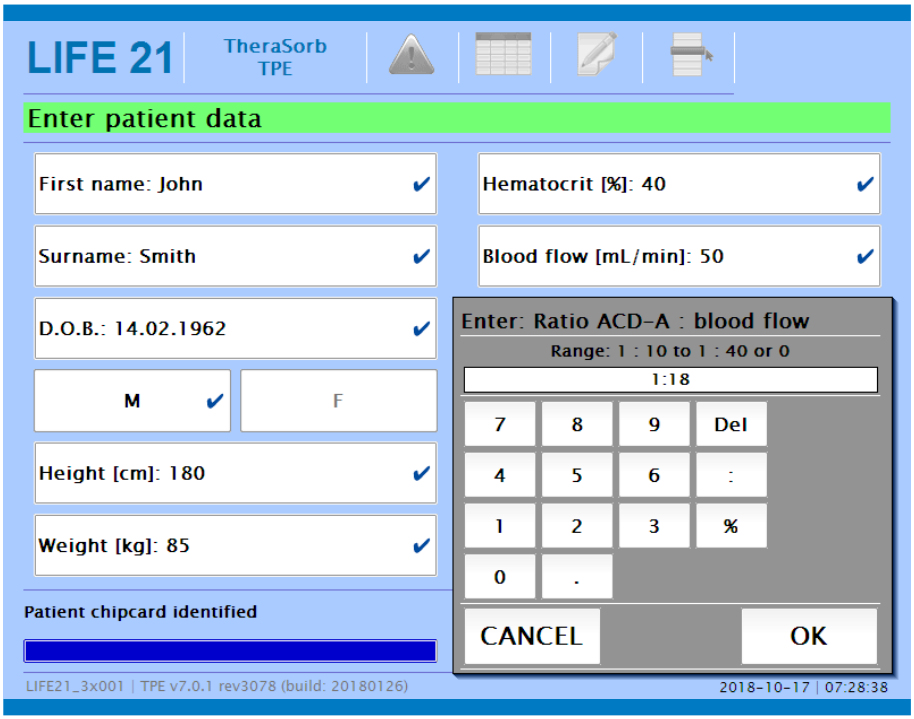
Operator action: After selecting the button **Anticoag. settings** make sure that further options are selected for entering and confirming relevant settings for anticoagulation (Screen 6.17). Settings for ACD-A (Screen 6.18 and Screen 6.19) and/or heparin (Screen 6.20) are required. ACD-A can be entered as the ratio of ACD-A to blood flow (e.g. 1:18) or in percentage to blood flow (e.g. 5%).

⚠ WARNING

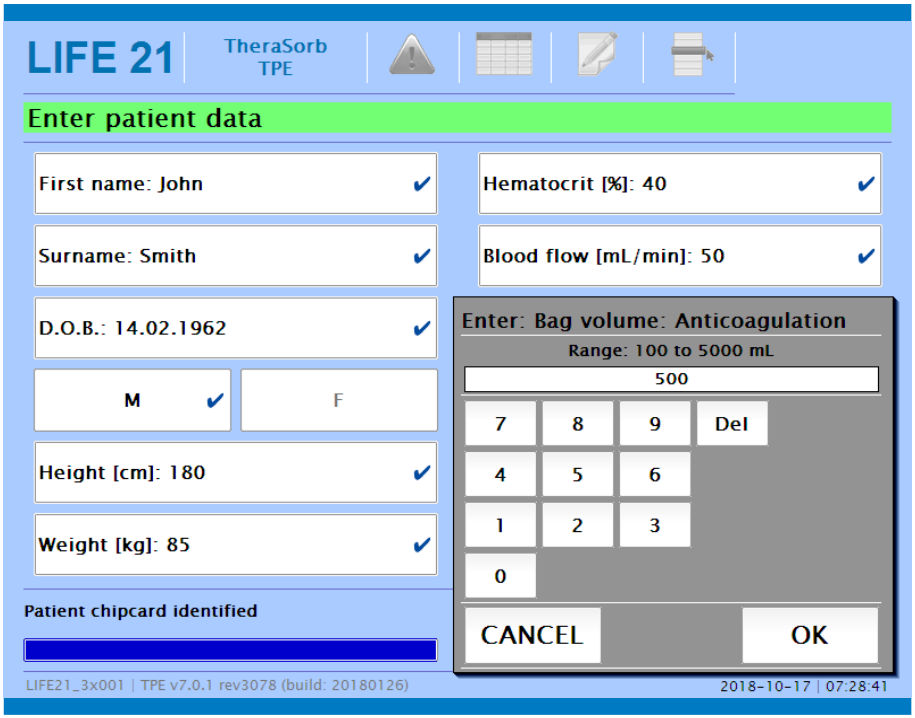
It is essential to read the recommendations for anticoagulation settings given in the LIFE 21 apheresis unit user manual "General instructions and troubleshooting". The LIFE 21 apheresis unit cannot monitor the connection of wrong or incorrectly concentrated anticoagulation solutions.If the patient experiences symptoms of hypocalcaemia (a risk if ACD-A is adminstered) countermeasures have to be taken (e.g. calcium administration). Refer to the LIFE 21 apheresis unit user manual "General instructions and troubleshooting" for details. The patient must be informed about symptoms of physiological reactions to citrate.



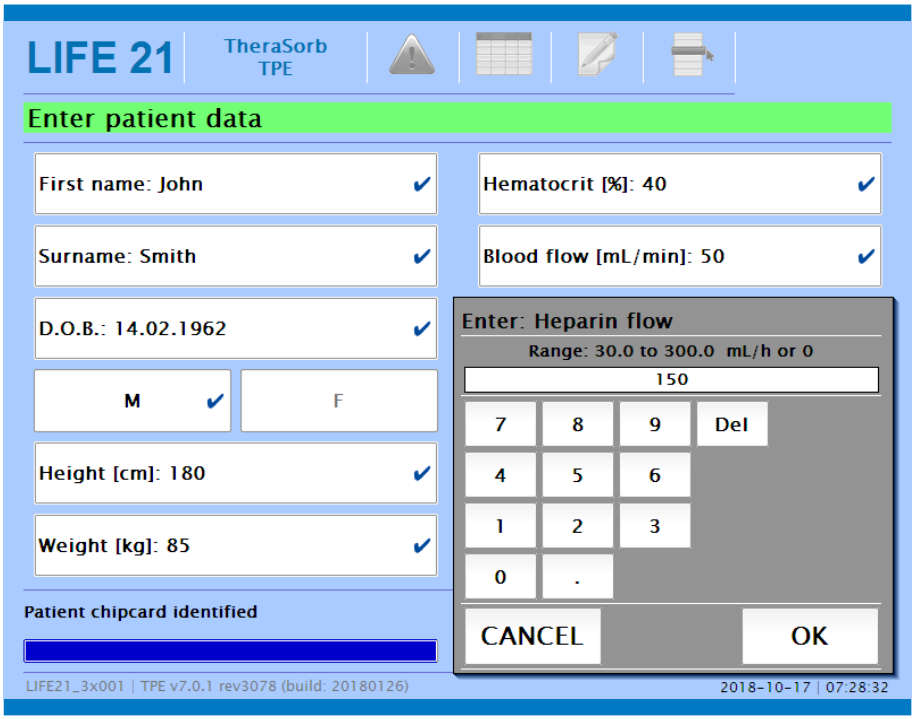
Screen 6.17: Anticoagulation settings



Screen 6.18: Ratio ACD-A to blood flow



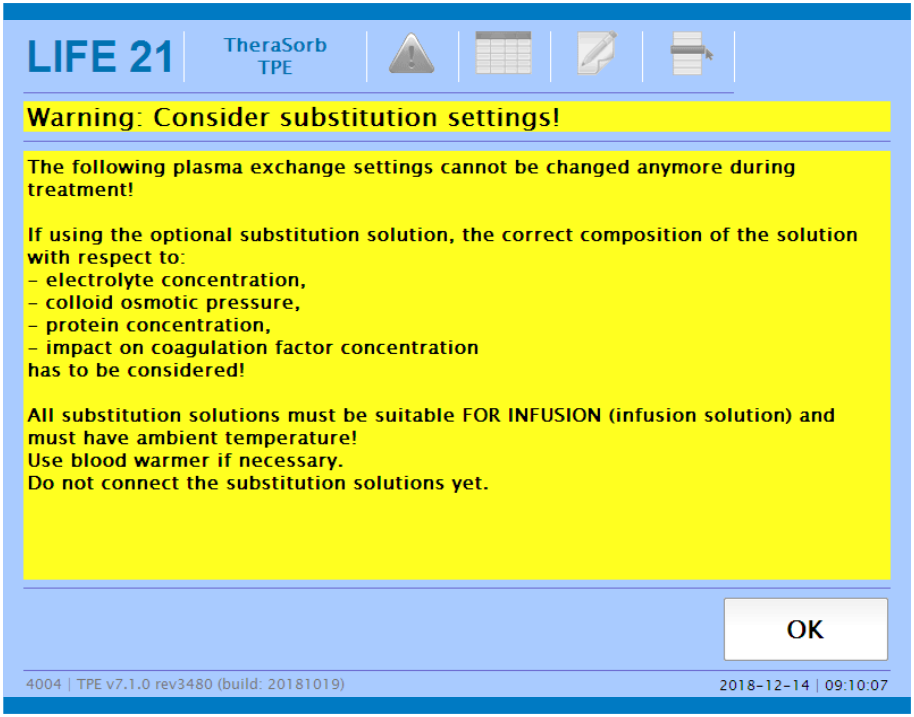
Screen 6.19: ACD-A bag volume



Screen 6.20: Heparin settings – flow rate

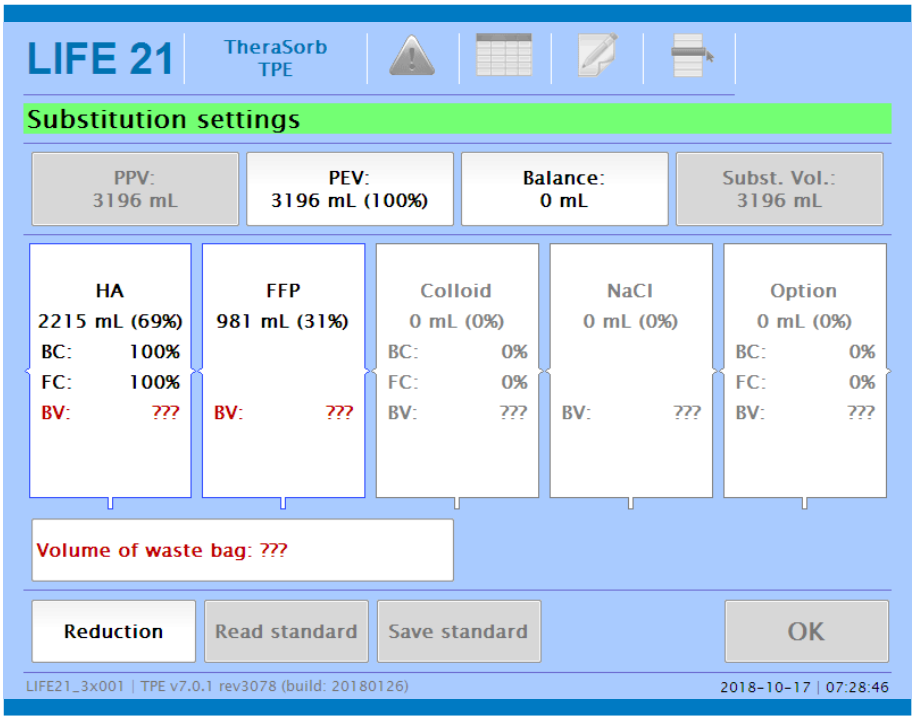
6.3.3 Substitution settings

Operator action: After selecting the button **Substitution settings** the follwing screen is displayed (Screen 6.21). Read the content carefully and continue by selecting **OK**.



Screen 6.21: Additional information about substitution settings

Operator action: After selecting the button **OK** all treatment-related parameters are displayed and must be entered by the operator (Screen 6.22). A summary and explanation of each button displayed on the screen can be found in Table 6.2.



Screen 6.22: Entry of substitution settings

The device displays the substitution setting as shown in Screen 6.22 by default. If a solution is not required (e.g. FFP) the value needs to be set to zero.

⚠ WARNING

Make sure to enter the correct values for volume (BV), basic (BC) and final (FC) concentration of substitution solutions. The manufacturer is not liable for faulty dilutions based on incorrectly entered values.

⚠ CAUTION

Refer to the recommendations of the treating physician regarding the chosen substitution solutions for the patient, and all related parameters.

A summary and explanation of each button displayed on the treatment-setting screen can be found in Table 6.2.

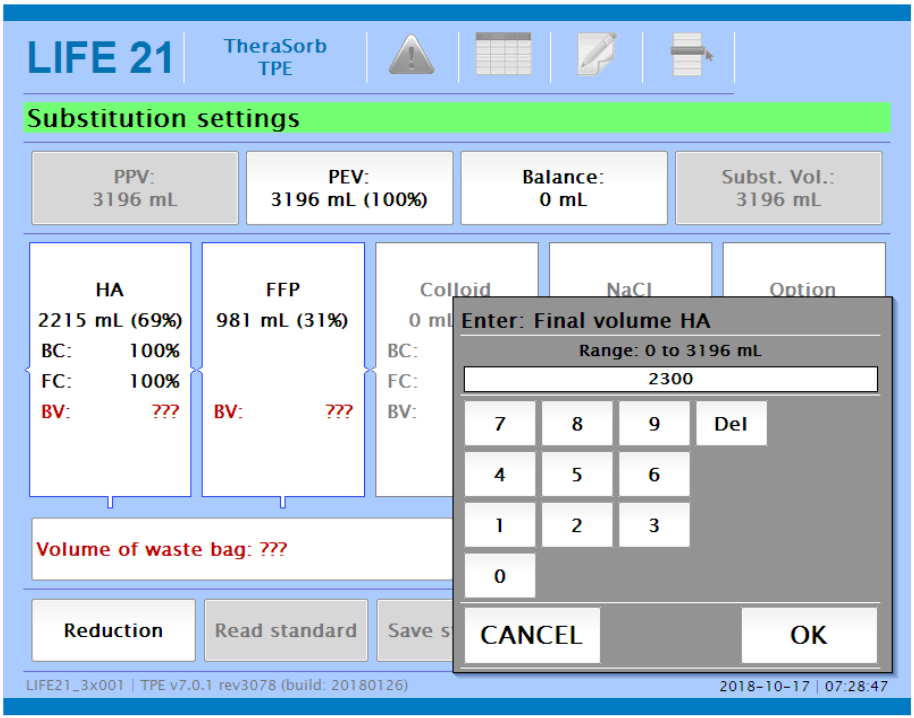
Button	Explanation
PPV	Patient Plasma Volume The amount of plasma in the patient's circulation is calculated by the LIFE 21 apheresis unit software based on gender, height, body weight. For patients younger than 12 years the age and hematocrit is used as well.
PEV	Plasma Exchange Volume The adjustable range of the plasma exchange volume is limited to ≤ 10% of the body weight.
Balance	The balance refers to the patient's fluid balance at the end of the treatment procedure. The balance can be set as follows: Hypovolemic: limited to –10% of Plasma Exchange Volume (PEV) Isovolemic, Hypervolemic: limited to +10% of Plasma Exchange Volume (PEV)
Subst. vol.	Total substitution volume Refers to the total volume of substitution solutions. If the total substitution volume is smaller or larger than the entered plasma exchange volume, the value will be depicted in red. The substitution solutions need adjustment before continuation of the process.
Substitution solutions:	The software diplays the following solutions by default:
HA	Human albumin: The permissible range of HA is limited to ≤100% of PEV + Balance.
FFP	Fresh Frozen Plasma The permissible range of FFP is limited to ≤100% of PEV + Balance
Colloid	Colloid solution The permissible range of Colloid is limited to ≤1.5% of body weight.
NaCl	0.9% sodium chloride: The permissible range of NaCl is limited to ≤2.8% of body weight.
Option	Optional solution, e.g. Ringer's solution The permissible range of the optional solution is limited to ≤100% of PEV + Balance.
Abbreviations used:	BC= basic concentration of the solution FC= final concentration after dilution by NaCl solution BV= bag volume of the solution
Volume of waste bag: ???	Handling of the waste has to be entered. Selection between three options: 10000 mL = standard bag, central = connection to central waste system or ??? = free input of bag volume, range 100…10000 mL

Button	Explanation
Reduction	Reduction curve with all treatment parameters is displayed
Read standard	Saved device-specific patient-independent settings from a previous treatment run can be retrieved from the apheresis unit as standard settings for the current treatment regarding substitution solutions, volumes, basic and final concentration, sequence of substitution solutions, bag volumes and waste bag volume. Settings can be modified and missing parameters should be entered. After confirmation, modified settings can be used as device-specific patient-independent setting by pressing **save standard**.
Save standard	The substitution settings are stored as device-specific and patient-independent standard and can be retrieved for further treatment runs by using **read standard**.
OK	By pressing the **OK** button the data entry is completed and not adjustable during the treatment!

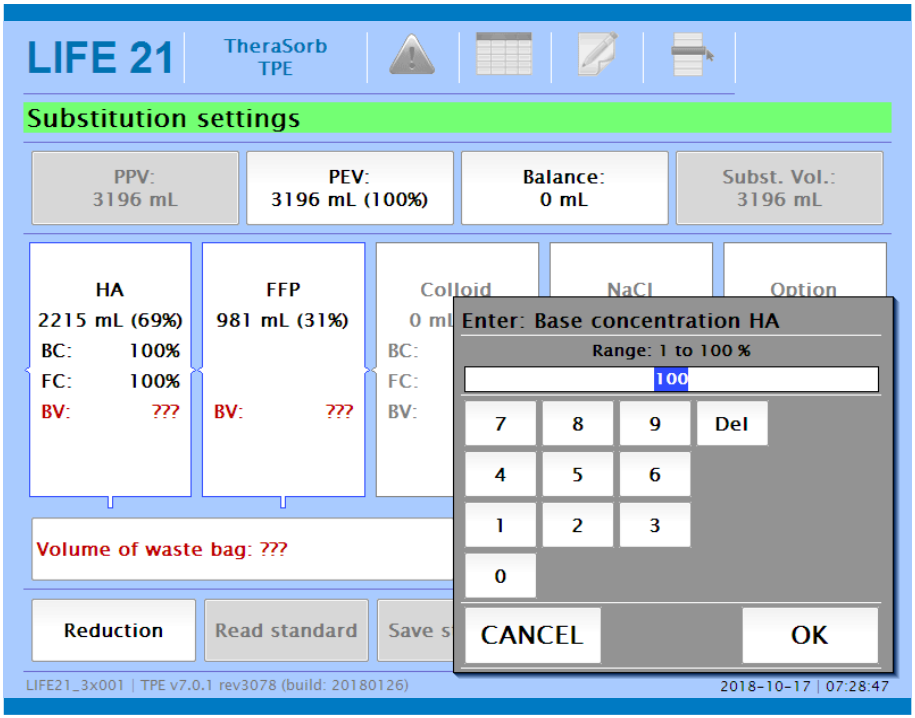
Table 6.2: Summary and explanation of displayed buttons for substitution settings

The parameter entry of the substitution solutions as described below uses the human albumin (HA) substitution solution as an example. All following substitution solution settings are entered accordingly.

Operator action: After selecting the field **HA**, all parameters must be filled out by the operator (Screen 6.23, Screen 6.24 and Screen 6.25). Press **OK** on the data entry mask of each screen to confirm the data and to continue to the next parameter entry mask.

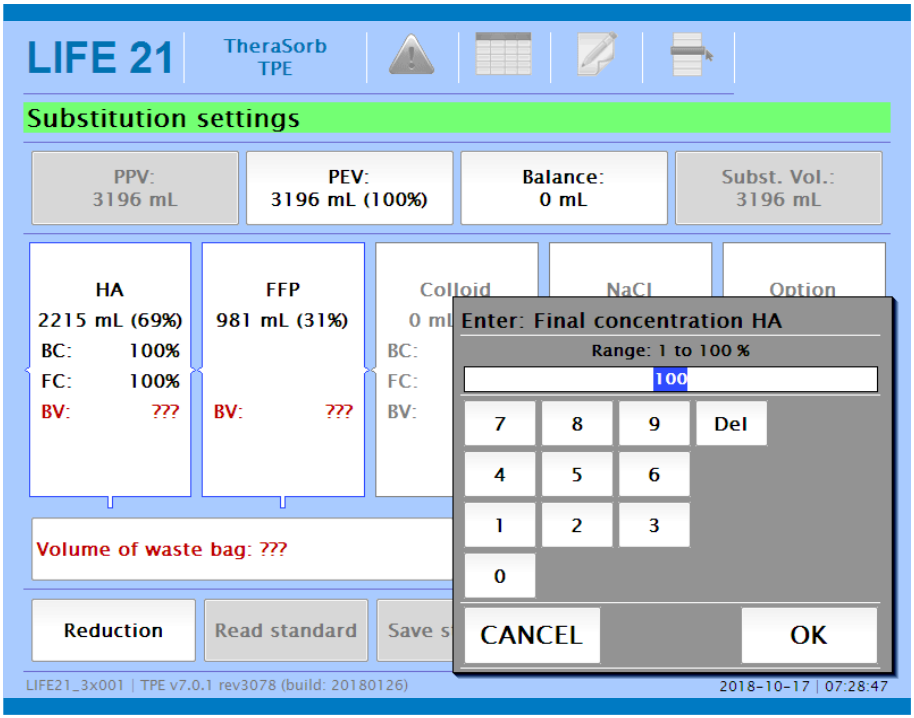


Screen 6.23: Representative screen for data entry – final volume of human albumin

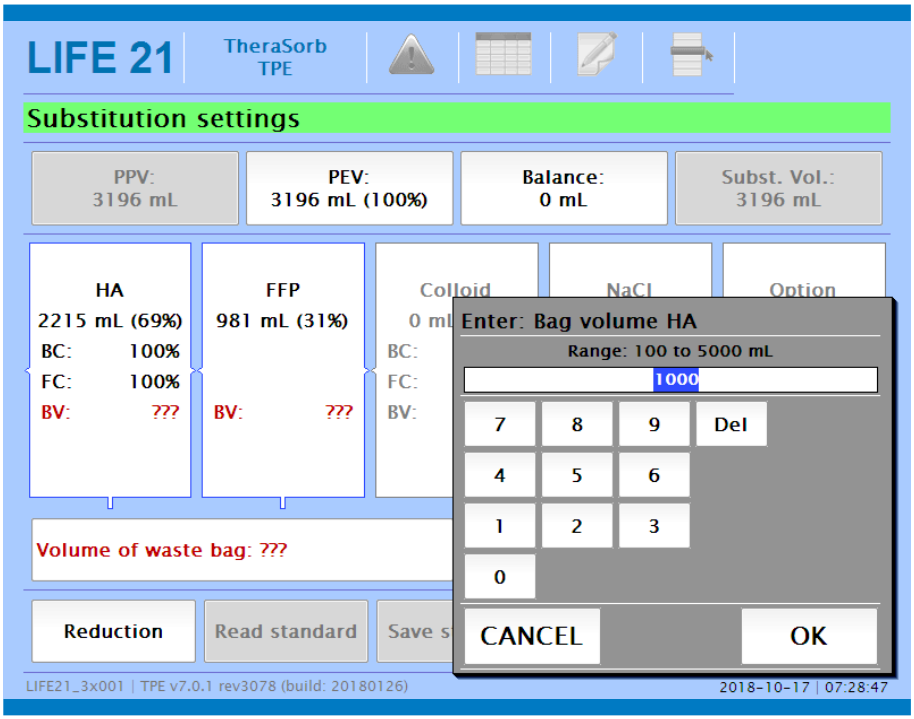


Screen 6.24: Representative screen for entry of basic concentration

If human albumin is used as substitution solution there is the possibility to dilute the concentration of this solution. For example, if the human albumin concentration in the bag is 20% (BC) and the requested final concentration is entered with 5% (FC), the device will automatically dilute the human albumin with NaCl solution. If the human albumin shall be infused without dilution, the value for base concentration (BC) is 100% and for the final concentration (FC) is 100%.

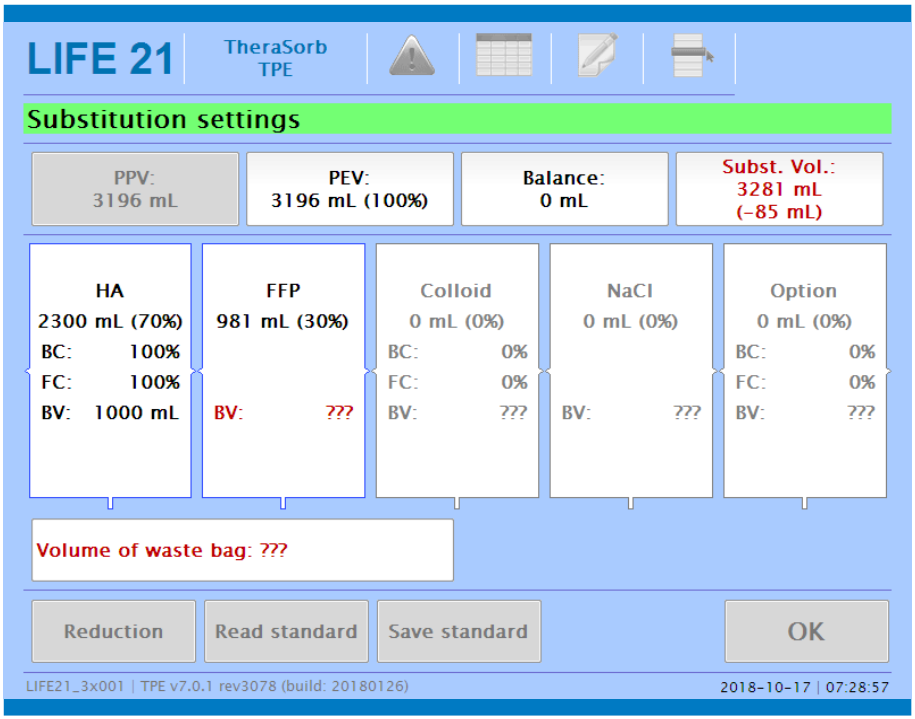


Screen 6.25: Representative screen for data entry – final concentration of human albumin

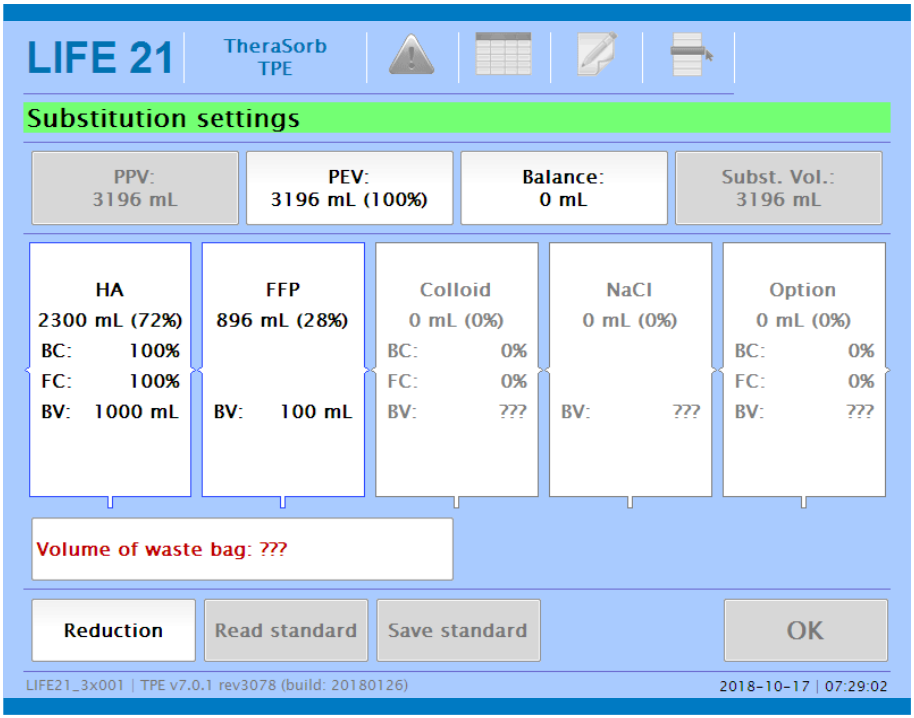


Screen 6.26: Representative screen for data entry – bag volume

In case of a discrepancy between the plasma exchange volume and the sum of all substitution solutions, the screen displays the total substitution volume in red (Screen 6.27). The volume to be added or reduced is given in brackets. The parameter then needs to be adjusted. In the example below the plasma exchange volume (PEV) and the final volume FFP were adjusted, and the parameters are in range (Screen 6.28).



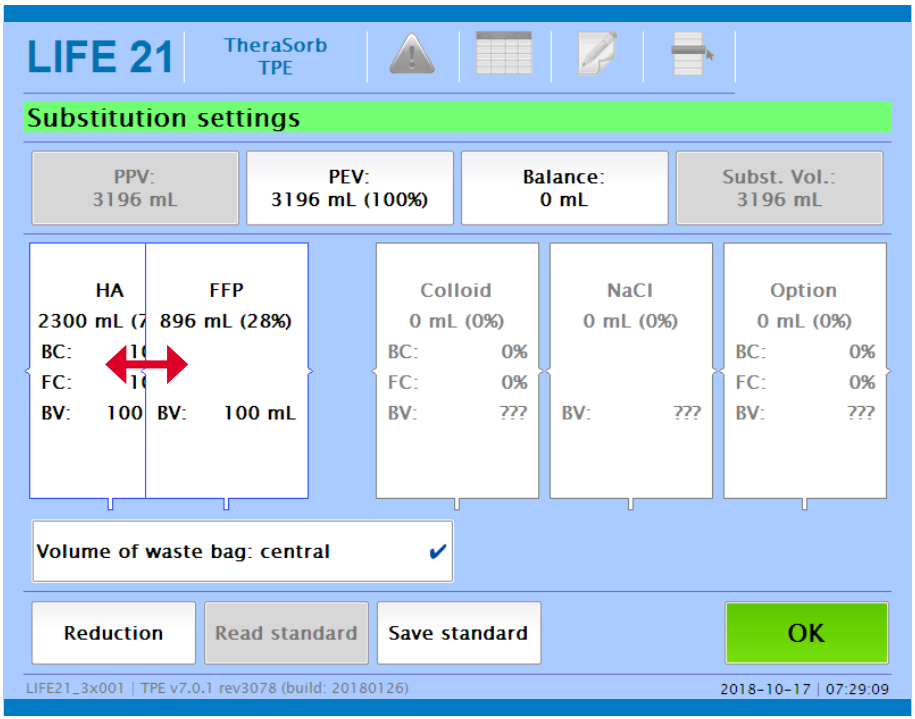
Screen 6.27: Substitution volume out of range (red display)



Screen 6.28: Substitution volume in range

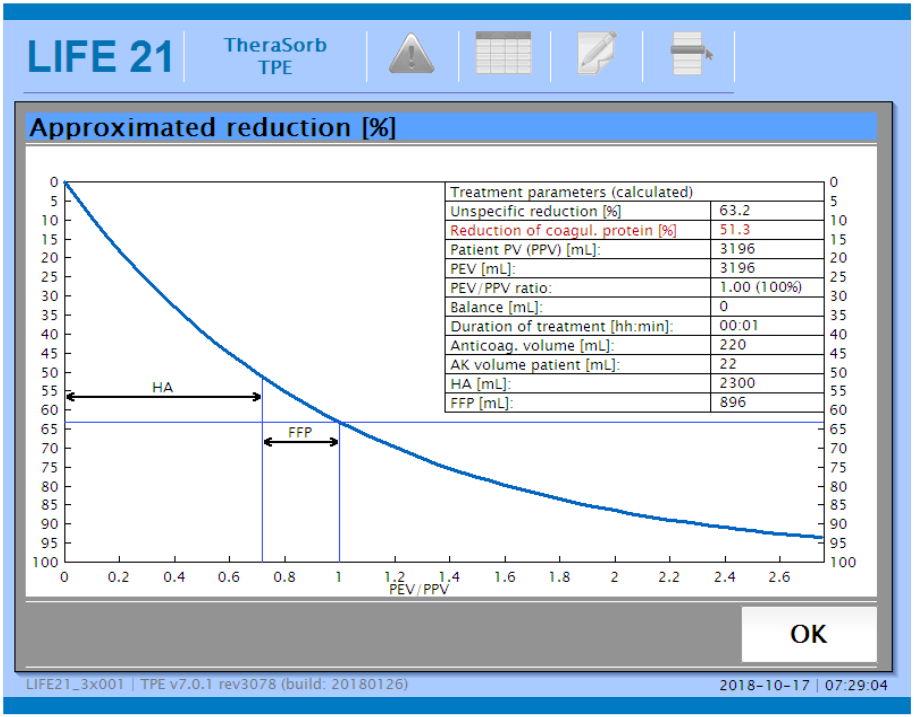
The sequence of the substitution solutions used for the patient can be changed by using the drag & drop functionality.

Operator action: Select the respective substitution solution field and move it to the desired position (Screen 6.29).



Screen 6.29: Change of substitution solution sequence

Operator action: After entering all remaining substitution solution settings, it is recommended to press the button **Reduction** to display the reduction and substitution curve and entered parameters for a final check of correctness (Screen 6.30).



Screen 6.30: Example of a removal and substitution curve

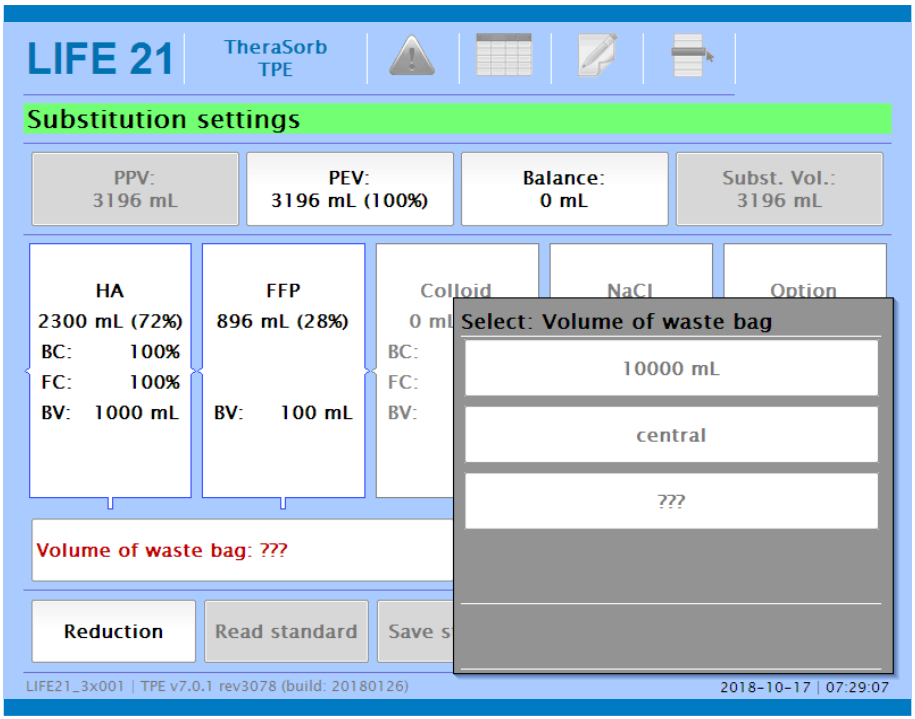
If the initial substitution setting leads to a critical reduction of the coagulation factors to less than 50% of the initial value, the appropriate parameter will be displayed in red. It is recommended to either lower the Plasma exchange volume (PEV) or to substitute, at least partially, with Fresh Frozen Plasma (FFP).

⚠ CAUTION

Coagulation factors can be reduced by more than 50% depending on the use of the chosen substitution solutions.

FFP as a substitution solution is already anti-coagulated with citrate and can have an influence on the anti-coagulation regimen. When planning the treatment, consider the potential risk of overdosing citrate if using ACD-A as anticoagulant. Refer to the LIFE 21 apheresis unit user manual "General instructions and troubleshooting" for more details.

Operator action: Press **OK** and select the button **Volume of waste bag: ???** and choose one option displayed on the screen (Screen 6.31).



Screen 6.31: Select filling volume of waste bag

After entering all substitution settings, the entries can be saved as a device-specific and patient-independent standard by pressing **Save standard**. For subsequent treatments (e.g. new patient) the button **Read standards** allows the operator to refer to the device-specific and patient-independent standard.

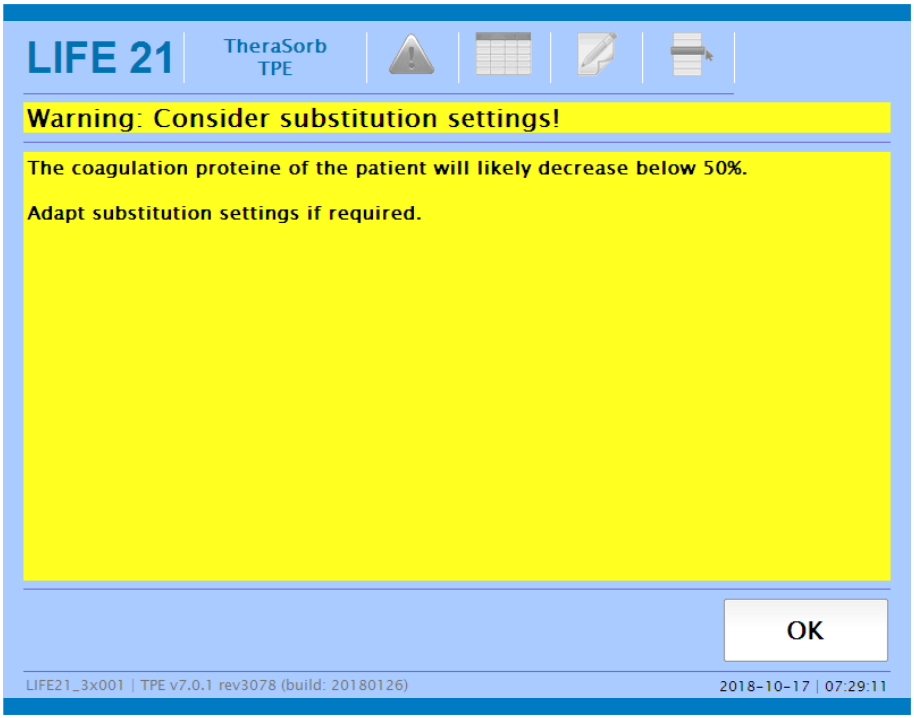
In case of consecutive treatments, parameters from the patient chip card will be displayed on the screen automatically. The data can be modified if needed. All parameters need to be confirmed. The substitution settings can be used as device standard by pressing **Save standard**. *In addition, the previously defined device-specific standard can be used as setting for the current patient by pressing* **Read standards**.

Operator action: Select the button **OK** on the main screen to leave the substitution setting screen and to return to the patient parameter screen (Screen 6.33).

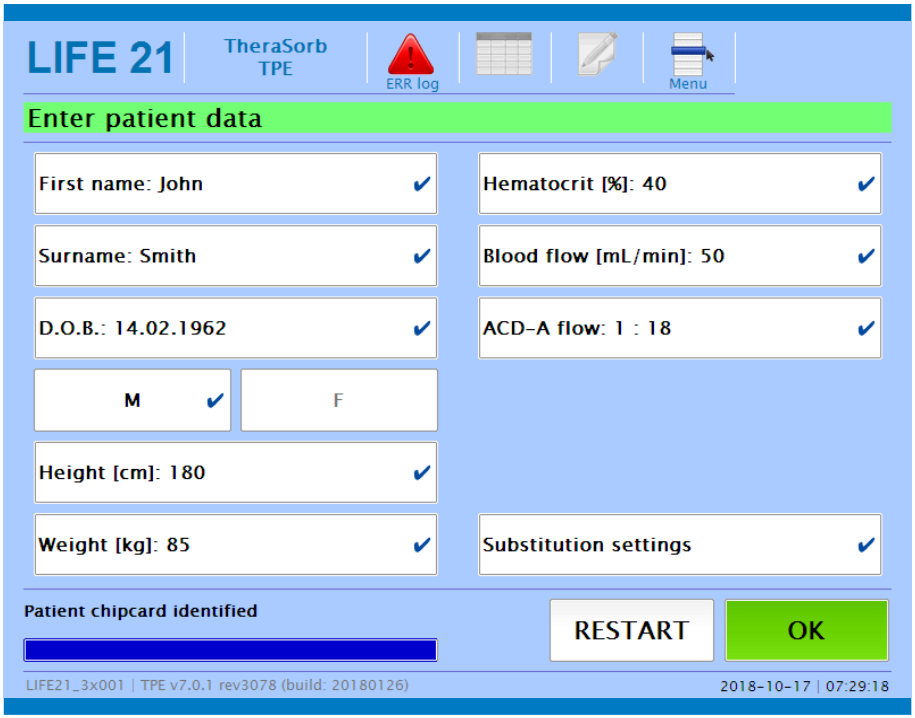
⚠ WARNING

Check settings for correctness before proceeding. It is not possible to change or adjust the substitution settings later on during treatment.

Operator action: After pressing **OK**, screens will be displayed to bring the operator's attention to important specifics (Screen 6.32). Continue the process by pressing **OK**.



Screen 6.32: Representative warning screen for substitutes used



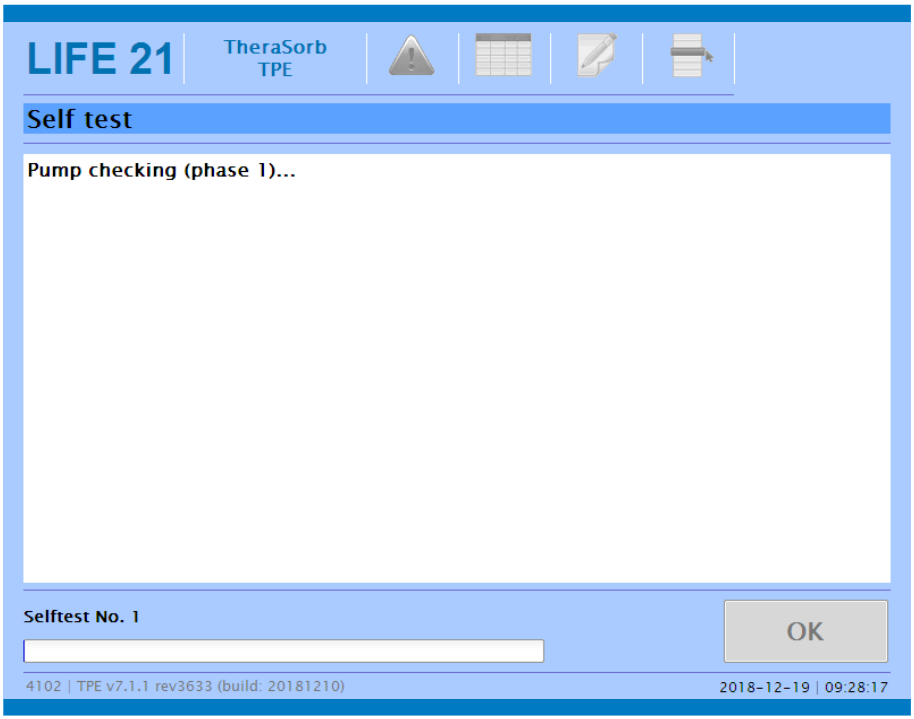
Screen 6.33: Completed patient parameter screen

Operator action: Press **OK** to start the next self-test phase of the LIFE 21 apheresis unit.

All patient-related settings will be transferred to the patient chip card and the device starts internal tests (Screen 6.34) before continuation.

⚠ CAUTION

Do not remove the chip card unless prompted by the device. Incorrect insertion or removal may lead to data loss or data corruption.



Screen 6.34: Status screen for device self tests

6.4 Tubing set installation – Part 2

The following chapter guides the operator through the tubing set installation – Part 2. Attachment of solutions, optional usage of blood warmer, as well as the connection of the patient to the tubing set are described.

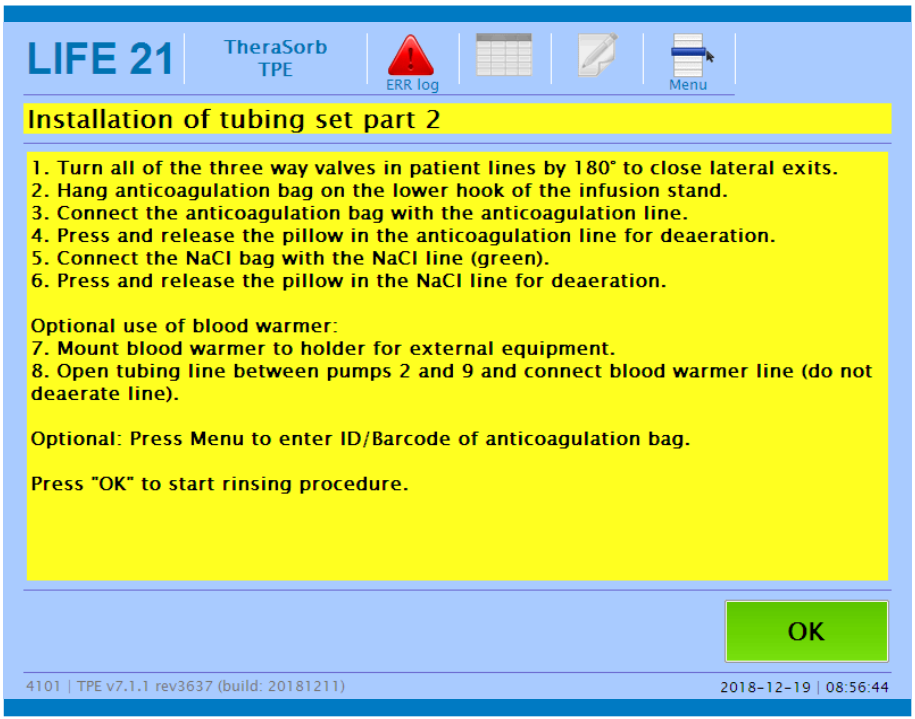
⚠ CAUTION

Observe adequate hygienic measures for aseptic handling for all preparative steps.

6.4.1 Connection of solutions

After device self tests have been completed, the overview screen for the second part of the tubing set installation is displayed (Screen 6.35).

Operator action: Follow the instructions on the screen for the connection of the solutions to the appropriate tubing lines.



Screen 6.35: Installation steps for part 2

Figure 6.7 shows the correct position of the 3-way stopcock after turning. The lateral exit can be used, for example, for a heparin infusion line. The injection port can be used, for example , for blood sampling or , if needed, to inject a bolus during the treatment.

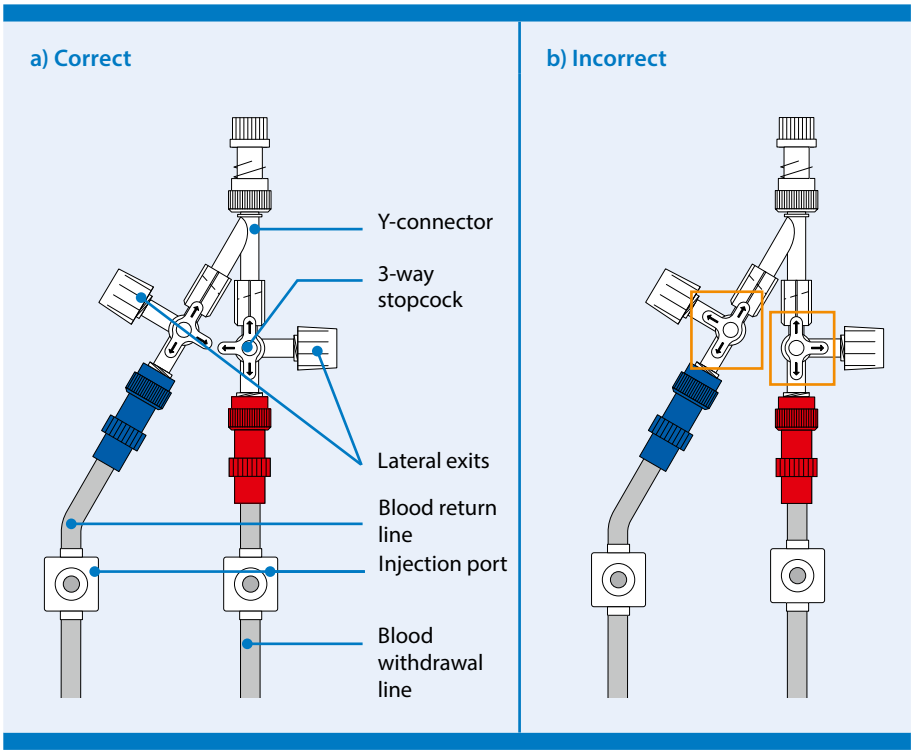


Figure 6.7: Correct position of the 3-way stopcocks

Before proceeding with the next steps, it is recommended that all solutions are brought to ambient temperature, and/or that a blood warmer is connected to the tubing set.

Operator action: Mount the blood warmer (e.g. ASTHOTERM PLUS or equivalent) to the holder for external equipment (Figure 6.8). Use a suitable single-use extension line with a volume of up to 100 mL (e.g. ASTOTUBE or equivalent). Open interconnected tubing between pumps 2 and 9 (Figure 6.9) and connect the fluid warmer extension line. After connection, the extension line is deaerated automatically and the volume is measured by the instrument.

⚠ CAUTION

Follow the manufacturer's instructions for the installation and use of the external blood warmer. Note that the blood warmer-related functionalities are not supervised by the LIFE 21 apheresis unit. Only the deaeration of the blood warmer extension line is automatically performed by the LIFE 21 apheresis unit. Miltenyi Biotec is not liable for incorrect use of the blood warmer

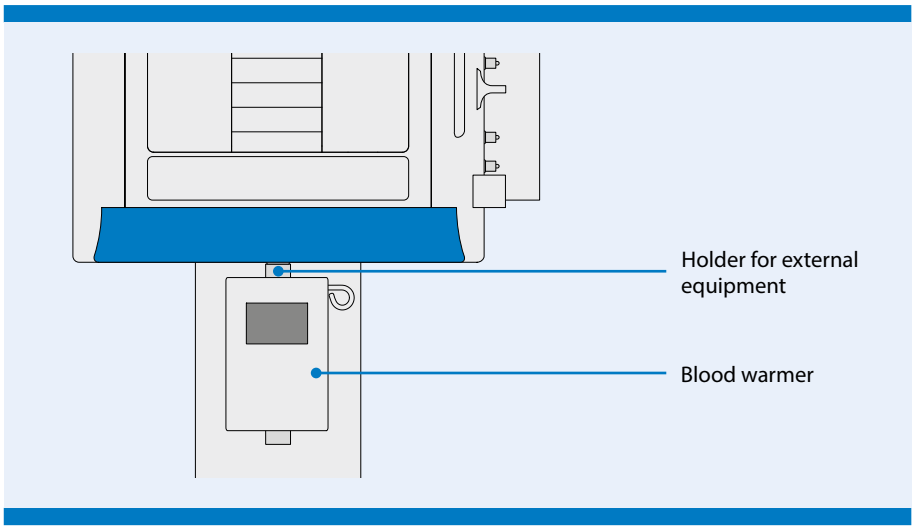


Figure 6.8: Connection of blood warmer

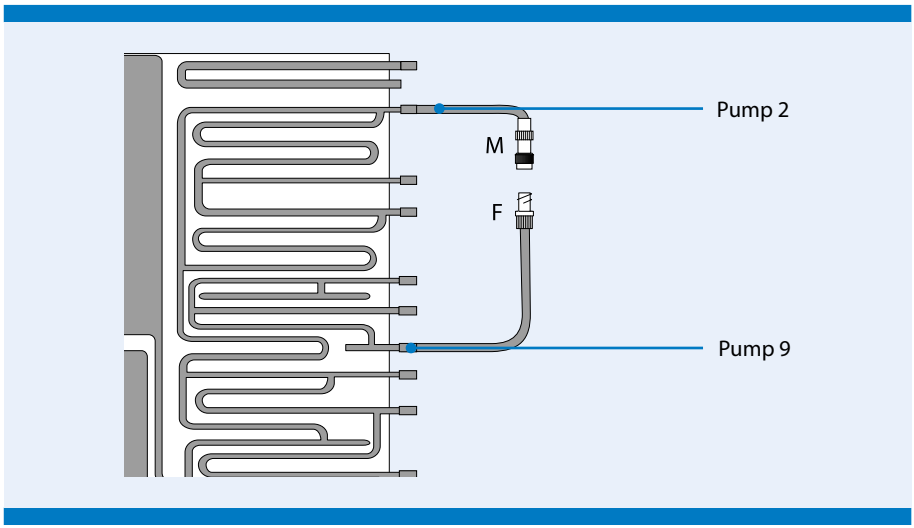
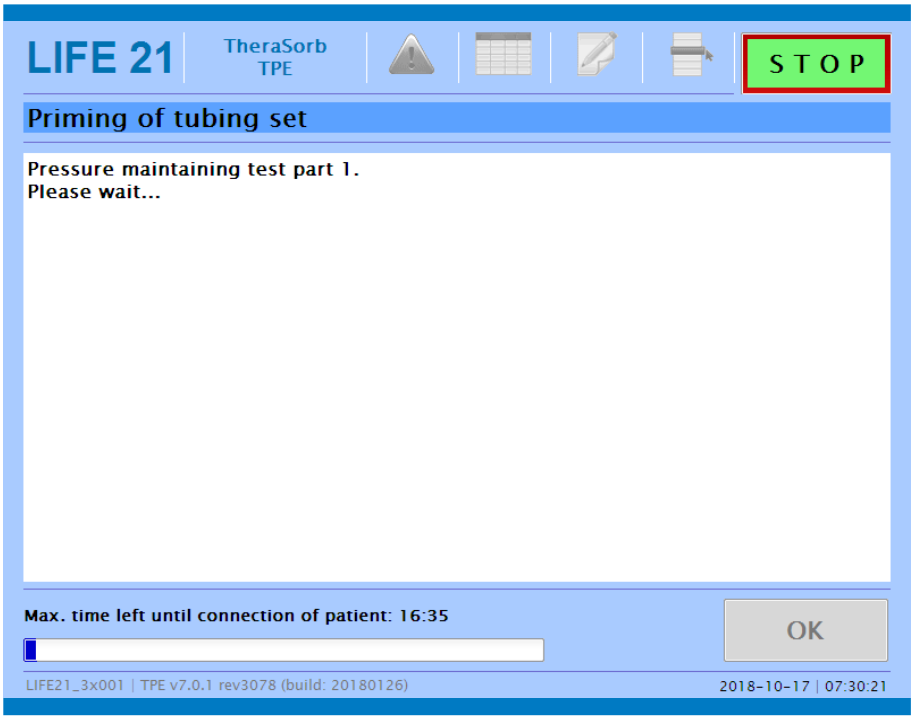


Figure 6.9: Connection of external blood warmer extension line to the tubing set

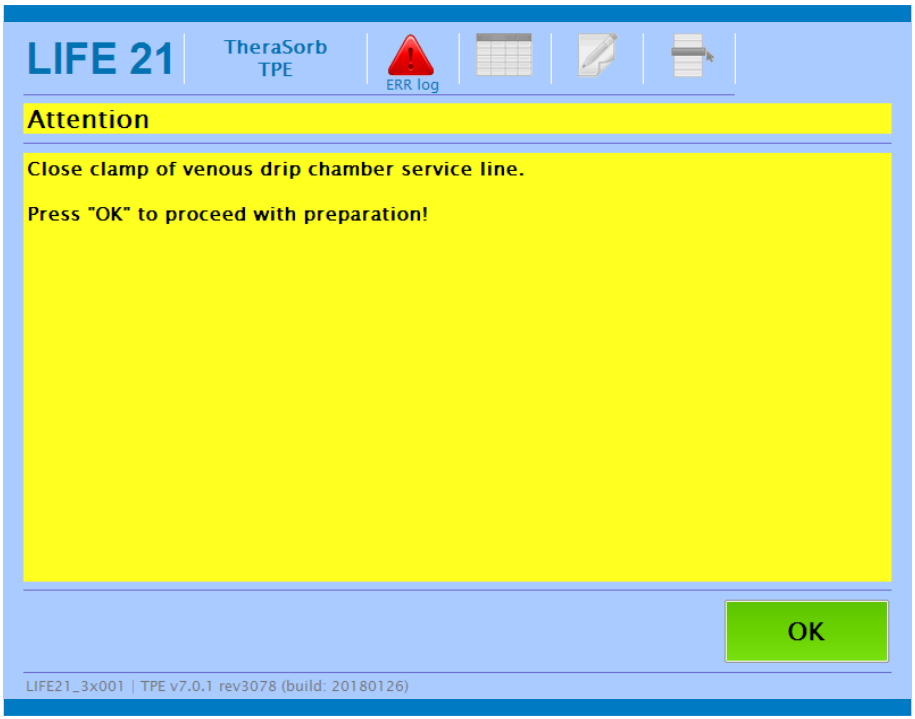
After pressing OK the priming of the tubing set starts and internal tests will be performed such as pressure tests, solution connection tests, followed by the removal of air in the single-needle chambers, patient line, disk separator, and the tubing set (Screen 6.36).



Screen 6.36: Priming of tubing set and self-tests

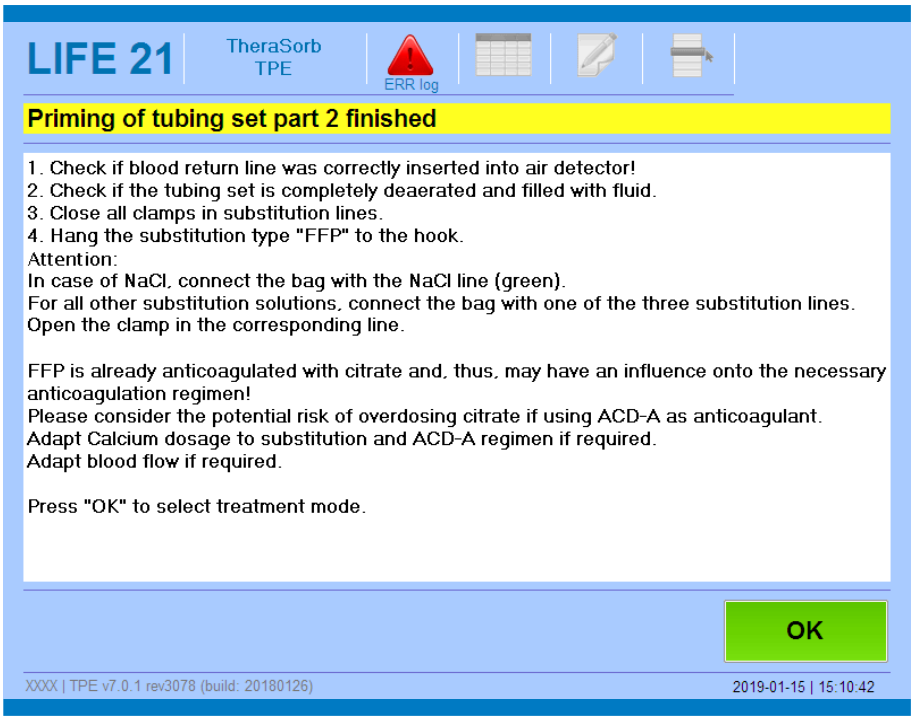
After successful completion of the tubing set deaeration, following screen is displayed (Screen 6.37)

Operator action: Close clamp on the service line of the venous drip chamber and continue by pressing **OK**



Screen 6.37: Closing of venous drip chamber service line clamp

Operator action: The screen (Screen 6.38) will be displayed. Follow the instructions on the screen and press **OK** to continue.



Screen 6.38: Check of correct insertion of patient return line and connection of first substitution solution

6.5 Connecting the patient

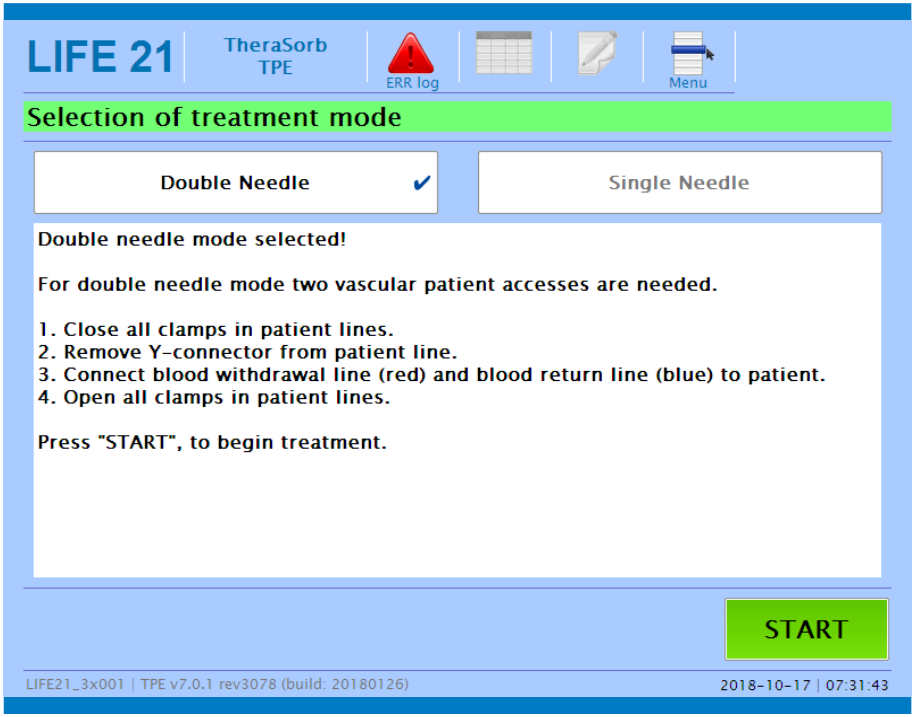
Operator action: The operator has to choose between double or single needle mode to connect the patient to the tubing set. For detailed information refer to the LIFE 21 apheresis unit user manual “General instructions and troubleshooting”.

Press **Double Needle** (Screen 6.39) or **Single Needle** (Screen 6.40) and follow the instructions on the screen.

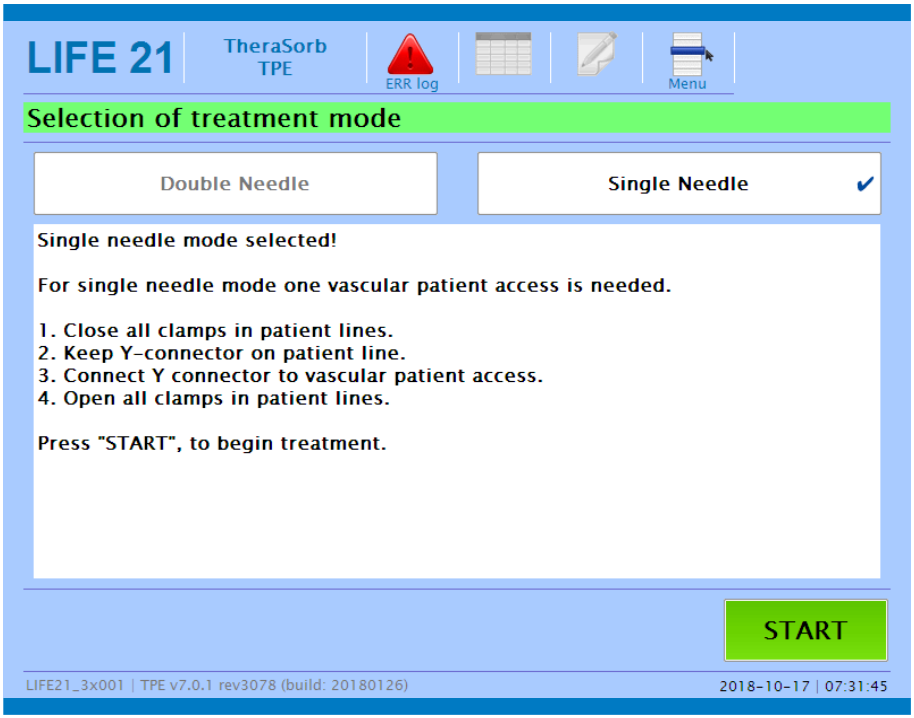
In case of the double needle mode, two independent venous accesses have to be established in the patient, and the Y-connector of the patient line needs to be removed (refer to Figure 6.7: Correct position of 3-way stopcock).

⚠ CAUTION

Patient access must be carefully monitored in order to avoid dislocation of the needles. To avoid inflammation and sclerotization of punctured veins, inject heparin bolus into the venous access, if required.



Screen 6.39: Instructions for double needle mode



Screen 6.40: Instructions for single needle mode

Operator action: Press START to begin the treatment.

⚠ CAUTION

Do not administer any other medication via the tubing set because of the risk of an interaction with the anticoagulant! The access points in the tubing set are to be used solely for sampling (for instance, to monitor the albumin concentration) during the treatment procedure.

7

Treatment run

The following chapter describes how the operator can adjust or change parameters related to the TPE procedure during the treatment run. The automated treatment run is divided into the following steps:

- Starting the pre-set blood flow for blood withdrawal
- Filling of extracorporeal blood circuit (patient lines and disk separator) with blood, reinfusion of NaCl solution into the patient (in this phase no plasma separation).
- Begin of plasma separation after complete filling of the disk separator with blood
- Separated plasma directed to the waste system
- Simultaneously, the substitution solutions are infused into the patient in the preset sequence, volume and dilution together with the blood cell concentrate from the disk separator.

⚠ CAUTION

During treatment, the patient must be monitored in order to ensure that any complications – including but not limited to the dislocation of the venous access – can be managed in a timely manner.

7.1 Treatment screen

During treatment, a status screen depicting the most important treatmentrelated information is displayed (Screen 7.1). Several submenus can be accessed from this screen to change parameters (e.g. blood flow). During the treatment the residual volume and residual time before the next necessary bag exchange is displayed in the **User action status information** of the treatment screen. If the remaining time is below 1 minute the status field will turn yellow.

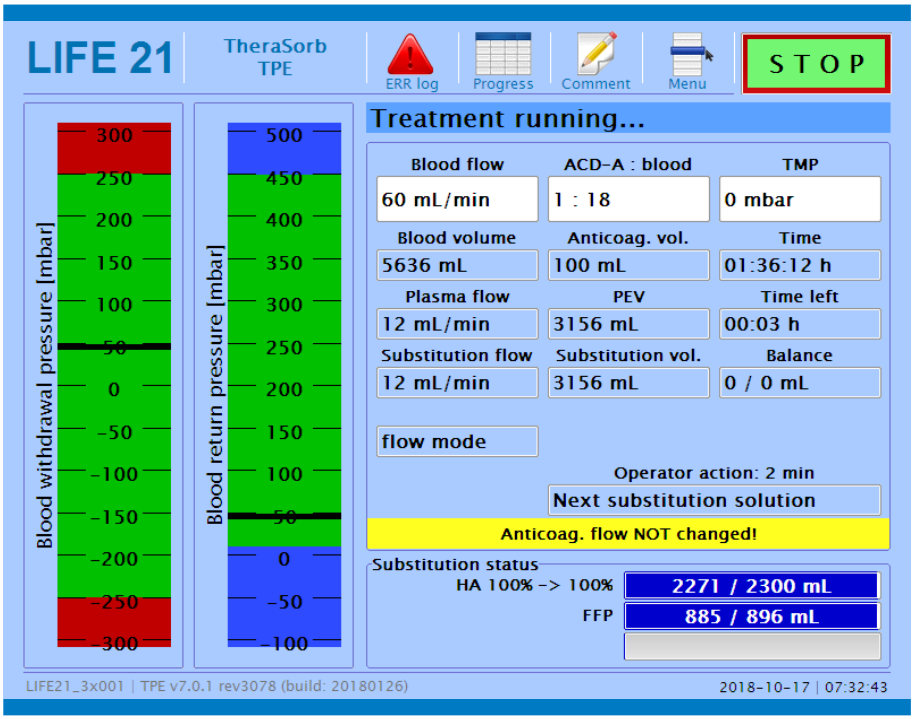
If an operator action is required, a screen prompting, the respective measure will overlay the treatment status screen.

If an error or malfunction occurs during treatment, an alarm screen accompanied by an audio signal will be displayed.

Refer to the LIFE 21 apheresis unit user manual “General instructions and troubleshooting” for details on alarm management, general instructions and troubleshooting.

⚠ CAUTION

Prolonged interruption of treatment may affect anticoagulation effectiveness and causes clotting in the extracorporeal fluid path.



Screen 7.1: Representative treatment status screen

A summary and explanation of each element displayed on the treatment status screen can be found in Table 7.1

Display element	Function
STOP	Allows to interrupt the treatment temporarily. All pumps are stopped. **This modus cannot be used for the exchange of the disk separator.**
RESTART	Continues a temporarily interrupted treatment.
MENU	Gives access to menu options (see chapter 7.3).
Comment	Opens a data entry screen for additional patient or treatment related data (e.g. blood pressure, pulse).
Progress	Displays a graph or a table with the progress of the treatment.
ERR log	Displays the list of errors of the current treatment.
Pressure bars	Displays the blood withdrawal pressure in the red bar. Blood return pressure is displayed in the blue bar. **Adjustment of parameters:** The allowed range for the withdrawal and return pressure is shown in green. The limits can be manually adjusted (upwards and downwards) by the drag and drop functionality. **Pressure monitoring:** The blood withdrawal and return pressures are monitored continuously by the device and are graphically displayed on the treatment screen. The user-defined permissible range is displayed in green, whereas areas outside of the range, which cause an alarm, are displayed in red or blue. The LIFE 21 apheresis unit automatically sets the alarm thresholds after a short start-up period. In the single needle mode (SN mode) only one bar is depicted, a red bar during the blood withdrawal phase and a blue bar during the reinfusion phase. The alarm range of blood withdrawal pressure and blood reinfusion pressure will be widened due to the following events: • on start of treatment, • after change of blood withdrawal flow, • after pressing STOP button, • after confirmation of an alarm and pressing the buttons CONFIRM and RESTART in an alarm screen.

Display element	Function
Blood flow	Displays the current blood flow rate and gives access to modify the blood flow rate.
ACD-A : blood flow respectively heparin flow	Displays and gives access to modify the ACD-A : blood flow ratio or the heparin flow, respectively.
TMP	Transmembrane pressure of the disk separator. Pre-defined settings should be followed. If needed the value can be adjusted manually.
Status information:	This information cannot be adjusted by the operator
Blood volume	= volume of blood processed
Anticoag. vol.	= volume of anticoagulant applied
Time	= elapsed time of treatment
Plasma flow	= current plasma flow
Plasma volume	= current plasma volume processed
Time left	= calculated remaining treatment time
Substitution flow	= flow rate of substitution solution to patient
Substitution vol.	= current substitution volume infused
Balance	= current balance situation
Flow mode respectively Pressure mode	"Flow mode" is set by default. Blood withdrawal is performed at the pre-set flow rate and an ALARM is set off if the defined upper or lower blood withdrawal or blood return pressure limits are exceeded. "Pressure mode" is shown in the status line if the corresponding mode is selected via MENU option. In pressure mode, the blood withdrawal rate is automatically adapted (increased or lowered) if the blood withdrawal pressure or blood return pressure reaches the upper or lower third of the allowed range (green coloured). Nevertheless, an ALARM is set off if the pressure reaches the limit of the allowed range despite of the flow rate adaption. Via the MENU button, the mode can be switched during the treatment.
User action status information	Displays residual time and residual volumes before next bag exchange is required. The background color changes to yellow if the time is below 1 minute.
Substitution status	Information about current substitution status (current and next two substitution solutions)
Yellow status line (not shown)	If the yellow status line is displayed, additional hints are given or an **operator action** is required.

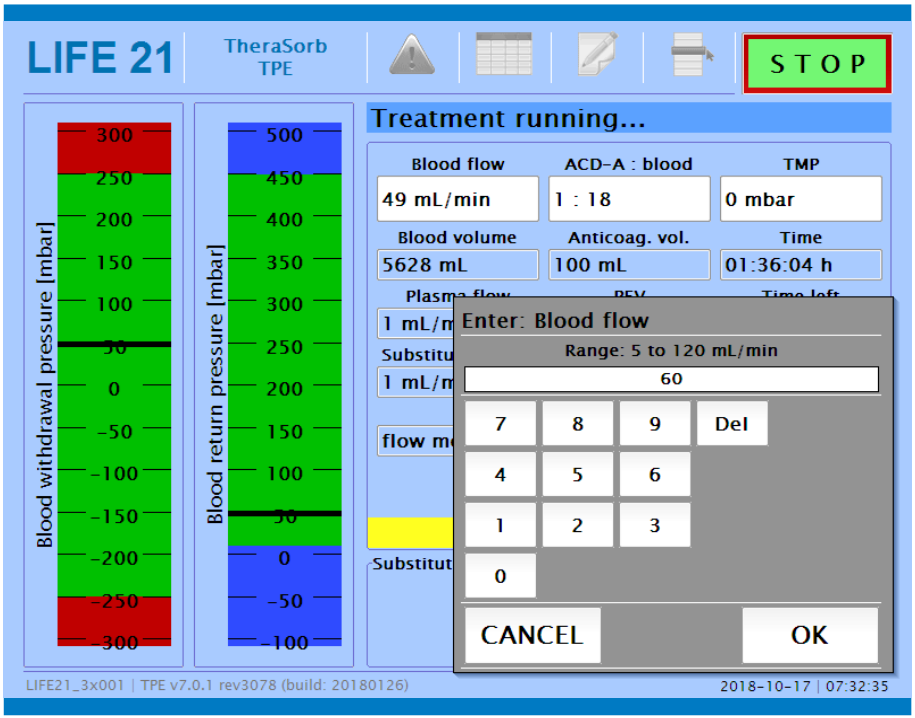
Table 7.1: Function of elements displayed on treatment status screen

7.2 Modification of main parameters

This chapter reflects the modification of parameters that might need attention during the TPE treatment. The program will accept only values in the permissible range displayed on the screen (refer to chapter 9 for details).

7.2.1 Modification of blood withdrawal flow

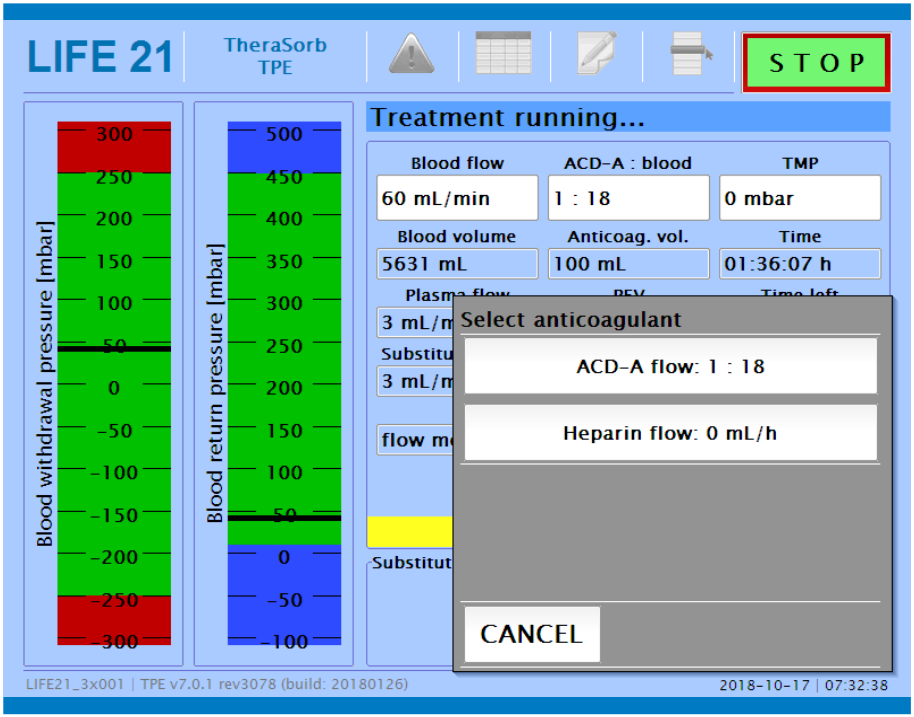
Operator action: Press **Blood flow** on treatment status screen to modify the blood flow to the required value (Screen 7.2). Press **OK** to return to the treatment status screen.



Screen 7.2: Representative data entry mask – blood flow

7.2.2 Modification of anticoagulant settings

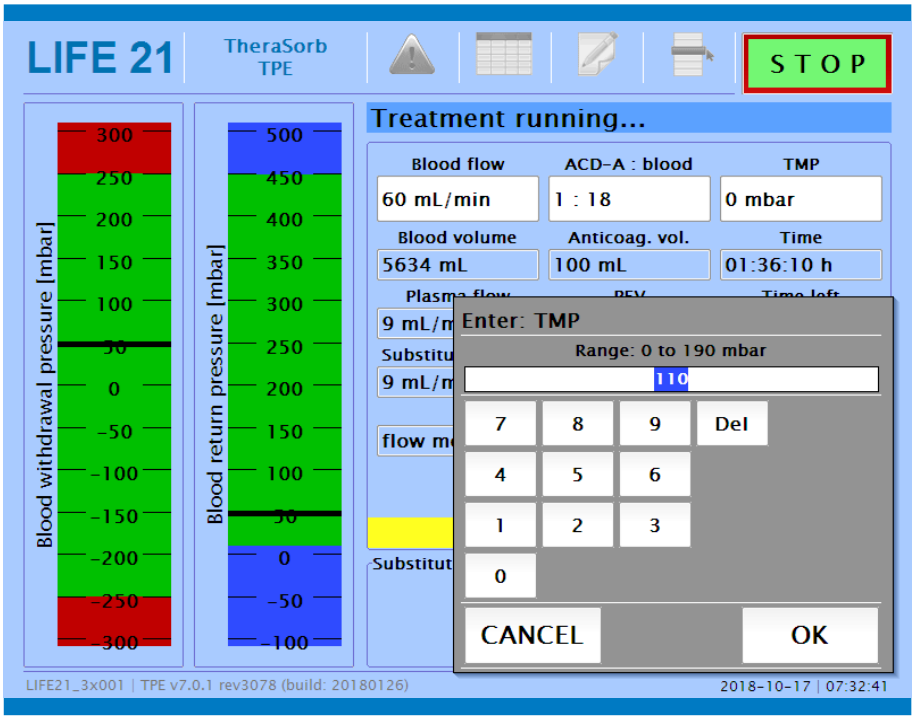
Operator action: Press **ACD-A:blood flow** on treatment status screen, select the anticoagulant setting and change the respective value (Screen 7.3).



Screen 7.3: Adjustment of anticoagulation settings

7.2.3 Modification of transmembrane pressure (TMP)

Operator action: Press **TMP** on treatment status screen and change the respective value (Screen 7.4).

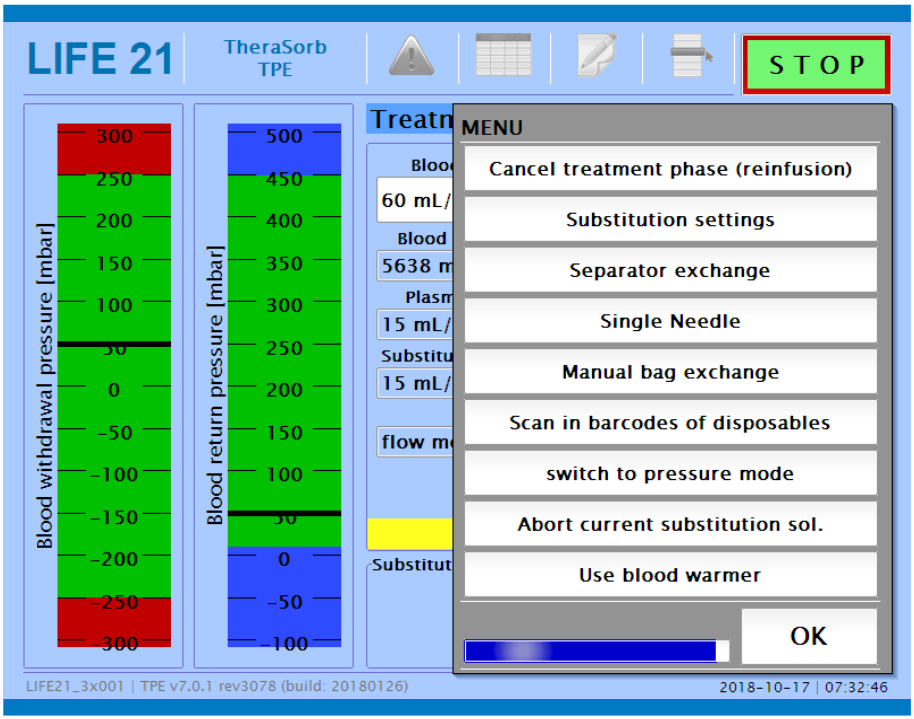


Screen 7.4: Modification of TMP value

The TMP is automatically adjusted to the value of the blood withdrawal flow. The operator is advised to follow the pre-defined settings.

7.3 Main menu

The menu screen is displayed after pressing the button **Menu** on the screen. It allows the operator to access more options, related to the current treatment run (Screen 7.5). A summary and explanation of each element displayed on the menu screen can be found in Table 7.2.



Screen 7.5: Representative menu screen

Display element	Function
STOP	Allows to interrupt the treatment temporarily. All pumps are stopped. **This modus cannot be used for the exchange of the disk separator.**
RESTART	Continues a temporarily interrupted treatment.
Cancel treatment phase (reinfusion)	Facilitates a premature abortion of the treatment and initiates the reinfusion phase. (see chapter 7.3.1)
Substitution settings	Facilitates the access to an overview about current substitution settings and the removal graph.
Separator exchange	Facilitates the exchange of the disk separator. **Do not exchange the disk separator in the STOP mode.** (see chapter 7.3.2)
Single Needle or Double Needle	Single Needle or Double Needle mode. (see chapter 7.3.3)
Manual bag exchange	Facilitates the manual bag exchanges of a bag of any kind during treatment. (See chapter 7.3.4)
Scan in barcodes of disposables (optional)	Opens sub-screen to enter different barcodes either by using the keypad shown or by using the barcode scanner. (see chapter 7.3.5)
Switch to pressure mode	Allows to change from flow mode to pressure mode. (see chapter 7.3.6)
Abort current substitution solution	Facilitates abortion of the current, and the switch to the subsequent substitution solution. The current substitution solution is aborted and the residual volume of the aborted solution will be infused automatically at the end of the treatment. (see chapter 7.3.7)
Use blood warmer	Facilitates the connection of a blood warmer extension line during treatment for heating the substitution solutions. (see chapter 7.3.8)

Table 7.2: Function of elements displayed on menu screen

7.3.1 Cancellation of treatment process

If a treatment needs to be canceled completely, the operator will be asked to return extracorporeal blood and plasma to the patient.

Operator action: Press **MENU** on treatment status screen. Press **Cancel treatment phase (reinfusion)** on menu screen. Press **YES** to abort the current treatment. The operator is asked to continue with the reinfusion phase. Refer to chapter 8 for details.

7.3.2 Exchange of the disk separator

In case the disk separator needs to be exchanged during treatment refer to the LIFE 21 apheresis unit user manual "General instructions and troubleshooting" for details.

7.3.3 Modification of treatment mode

To change the treatment mode from single to double needle and vice versa refer to the LIFE 21 apheresis unit user manual "General instructions and troubleshooting".

7.3.4 Manual bag exchange

Operator action: Press **MENU** on treatment status screen. Press **Manual bag exchange** on menu screen.

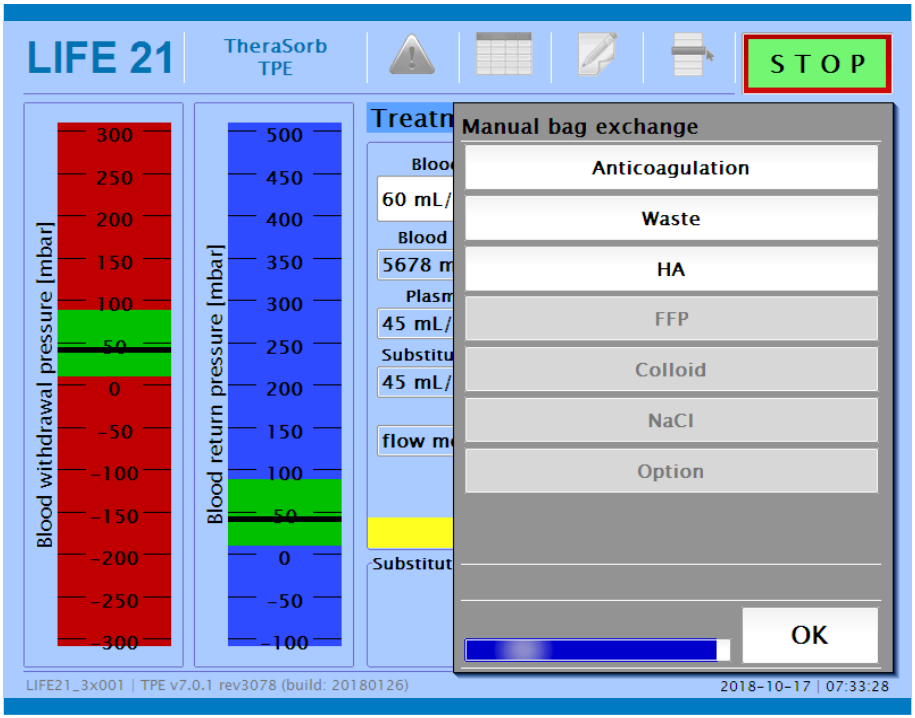
To exchange a substitution solution bag press the appropriate button (e.g. **HA**) and follow the instructions (Screen 7.6). Only the bag of the currently applied substitution solution can be exchanged.

To exchange the Anticoagulation bag press «**Anticoagulation**» and follow the instructions.

To exchange the NaCl bag press **NaCl** and follow the instructions.

To exchange the Waste bag press **Waste** and follow the instructions.

Make sure the selected bag is exchanged within the standby time given by the device. Press **OK** to move back to the treatment status screen.



Screen 7.6: Manual bag exchange

7.3.5 Barcode scan of disposables

The barcodes of disposables, for example solutions, can be entered.

7.3.6 Flow mode/pressure mode

For a description of this MENU option see Table 7.1.

7.3.7 Abort of current substitution solution

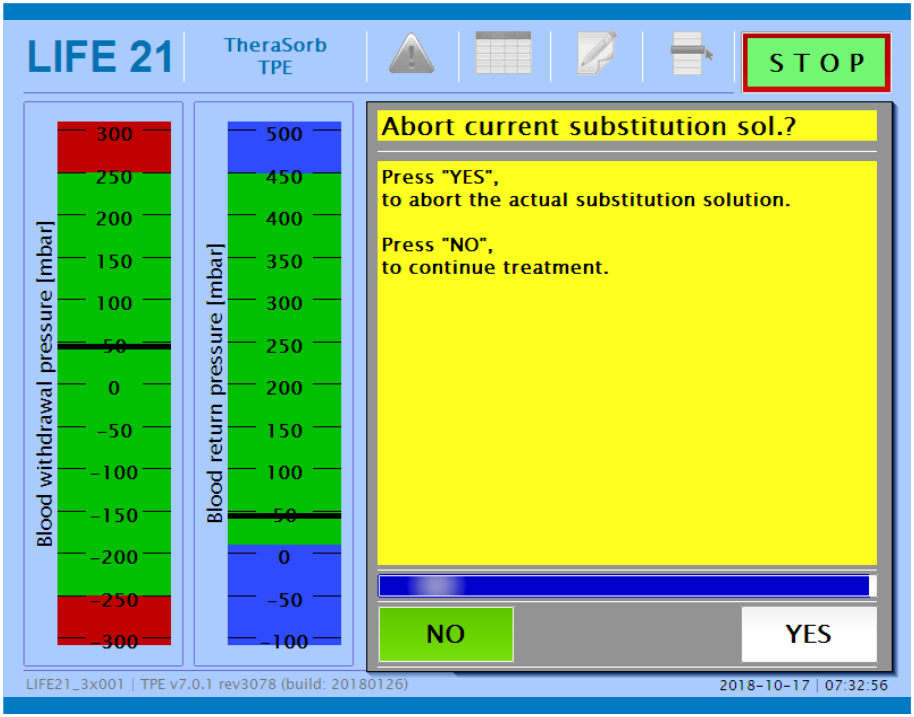
The operator is able to change the order of the previously defined substitution solutions (chapter 6.3.3) by aborting the current substitution solution. The residual volume of the aborted solution will then be automatically infused at the end of the treatment.

Operator action: Press **MENU** on treatment status screen. Press **Abort current substitution sol.** on menu screen. Press **YES** to abort the current substitution solution bag (Screen 7.7).

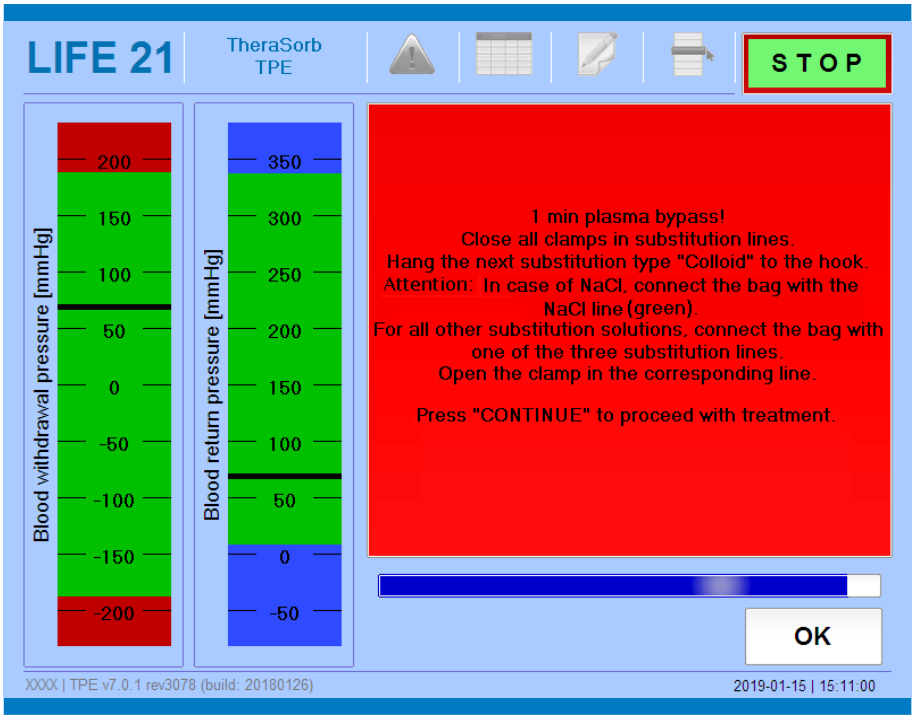
The substitution pump is stopped and the standby screen is displayed. The next substitution solution needs to be connected, for example, FFP (Screen 7.8).

Press **OK** to go back to the treatment status screen.

The device automatically continues with the newly attached substitution solution.



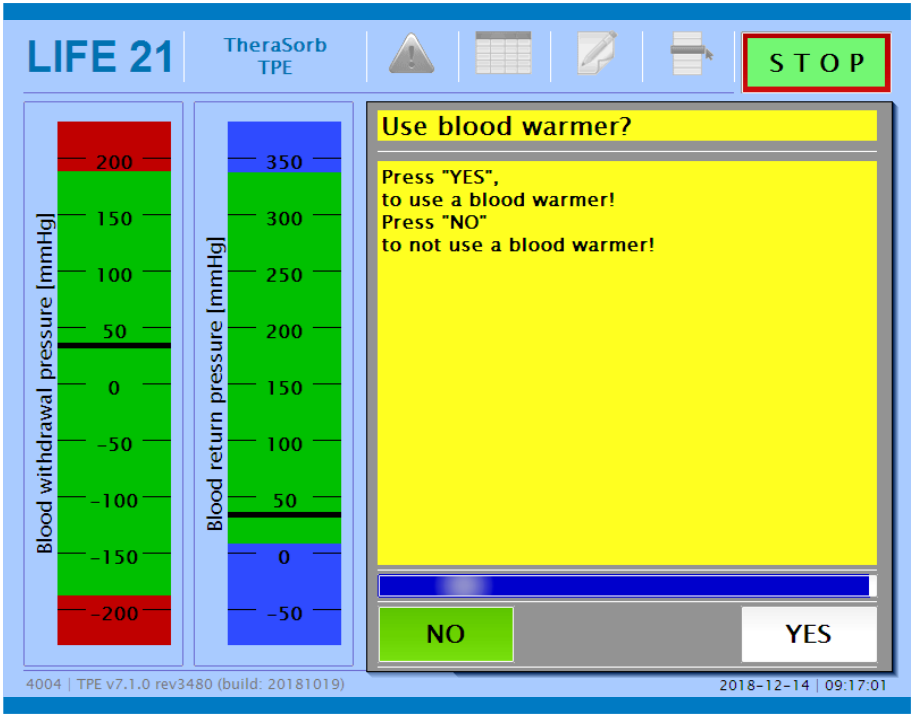
Screen 7.7: Abortion of current substitution solution



Screen 7.8: Connection of subsequent substitution solution

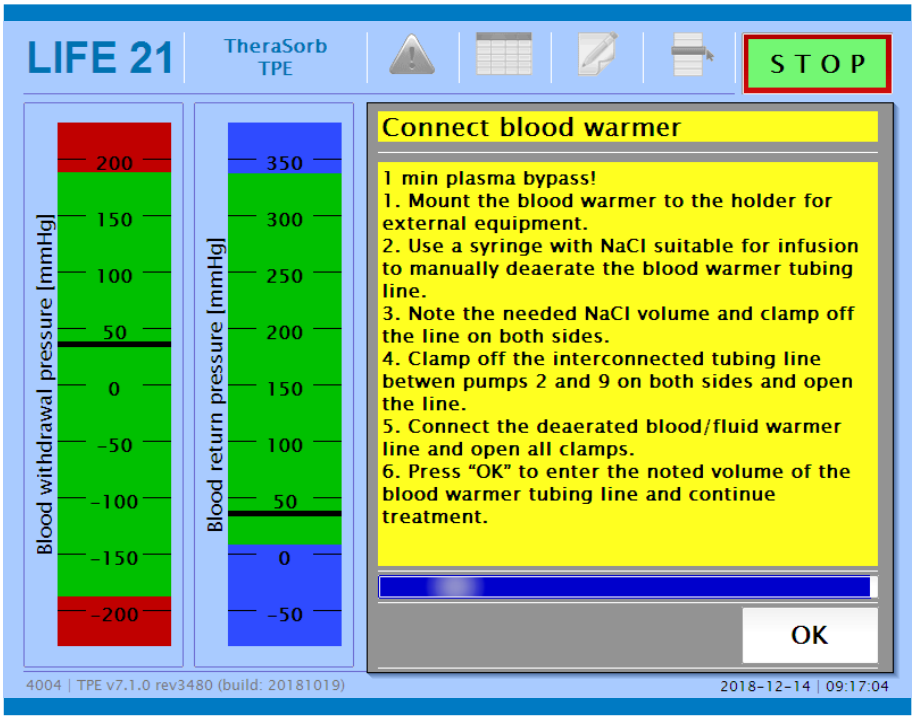
7.3.8 Use of blood warmer (optional)

Operator action: If it is necessary to connect a blood warmer during the treatment, press **Use blood warmer**. The following screen (Screen 7.9) will be displayed.



Screen 7.9: Confirmation screen to install blood warmer

Operator action: Press **YES** to continue and follow the instructions on the screen (Screen 7.10). Refer to Figure 6.8 and Figure 6.9 (chapter 6.4.1) for the connection of the blood warmer tubing line to the tubing set. Press **OK** to go back to the treatment status screen.



Screen 7.10: Instructions to connect blood warmer

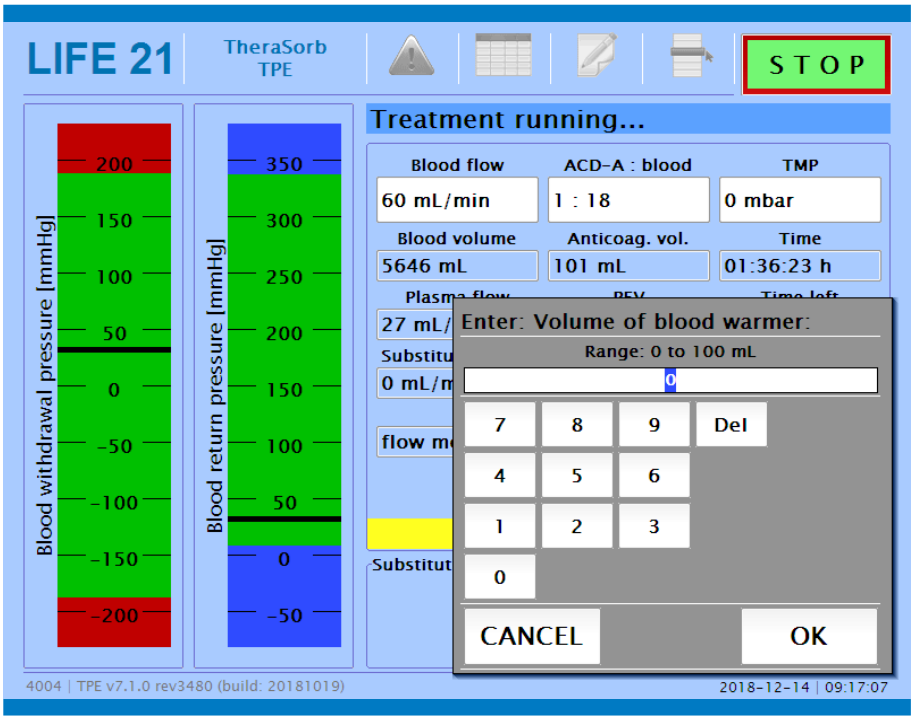
⚠ WARNING

Please make sure that the extension line is completely deaerated!

⚠ CAUTION

Follow the manufacturer's instructions for the installation and use of the external blood warmer. Note that the blood warmer-related functionalities are not supervised by the LIFE 21 apheresis unit. Miltenyi Biotec is not liable for incorrect use of the blood warmer.

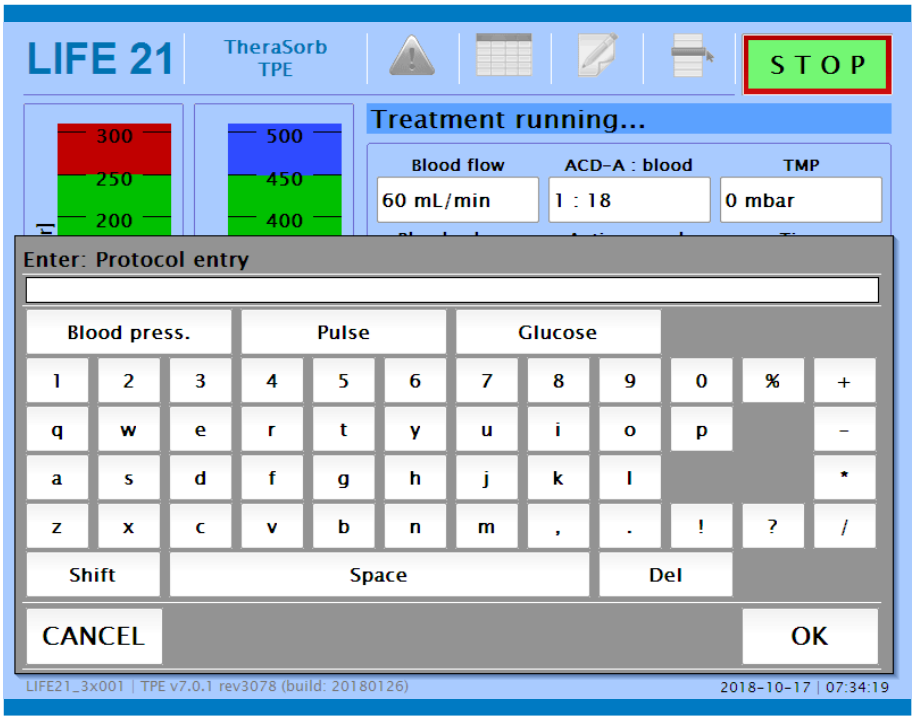
Operator action: After selecting **OK** the screen (Screen 7.11) will be displayed. Enter the noted volume used to deaerate the tubing line of the blood warmer and press **OK**.



Screen 7.11: Entry of volume of blood warmer tubing line

7.4 Comment input

Operator action: Press **Comment** button in treatment main screen (Screen 7.1). Press one of the pre-set comment functions (**Blood pressure**, **Pulse**, **Temperature**) and add the measured patient value or enter a free alphanumeric comment string (up to 80 characters).



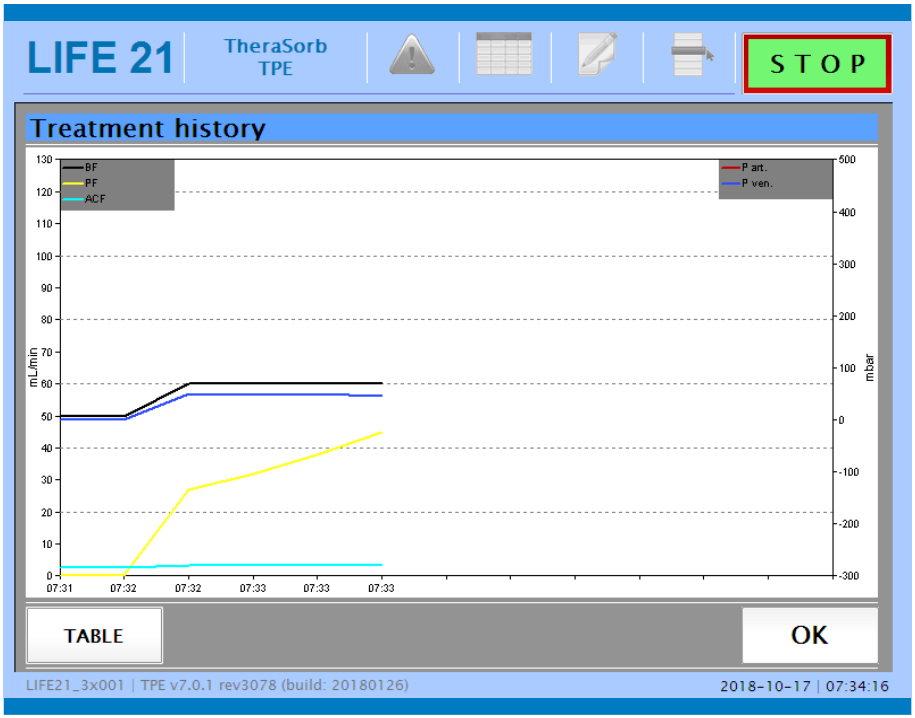
Screen 7.12: Comment input screen

7.5 Treatment progress

Operator action: Press **Progress** button in treatment main screen (Screen 7.1). A tabular or graphic view of the course of the following patient/treatment parameter can be shown:

- Blood flow
- Plasma flow
- AC flow
- TMP (only tabular view)
- Blood withdrawal pressure
- Blood return pressure
- Total flood volume (only tabular view)
- Total plasma volume (only tabular view)

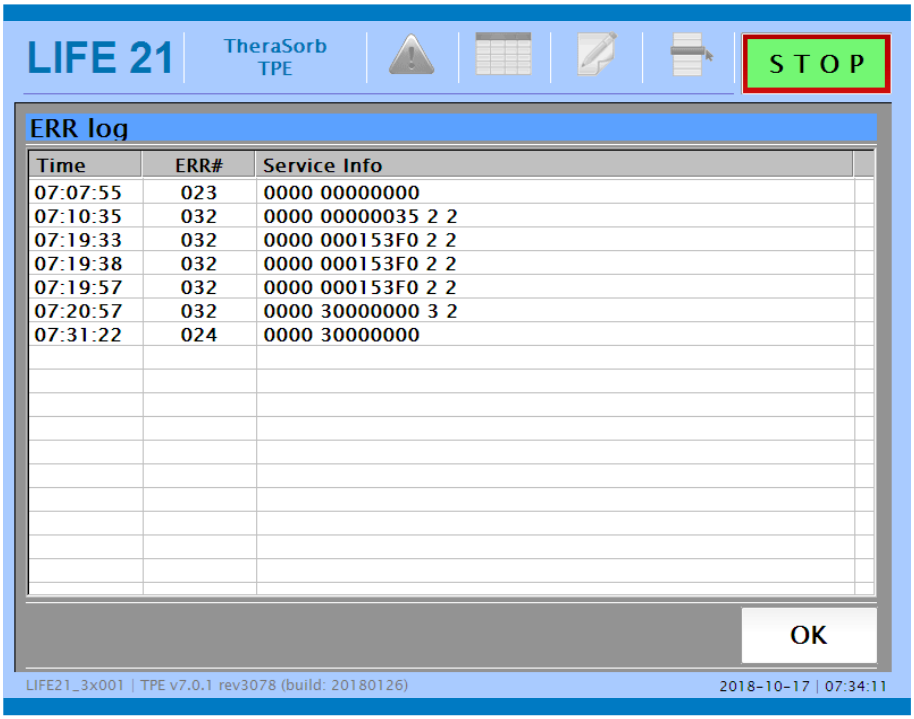
Select **GRAPH**/**TABLE** button to switch between the different views. Select **OK** to finish the treatment progress option and return to treatment main screen.



Screen 7.13: Treatment progress screen

7.6 Error logging

Operator action: Press **ERR log** button in treatment main screen (Screen 7.1). A tabular view of all alarms occurred during current treatment run is shown. This menu option is useful if an alarm ID shall be reported to customer service and the alarm ID could not be noted down in the moment where the error occurred. Note down the respective alarm ID and the corresponding Service Info.



Screen 7.14: Error log screen

8

Reinfusion and shut down process

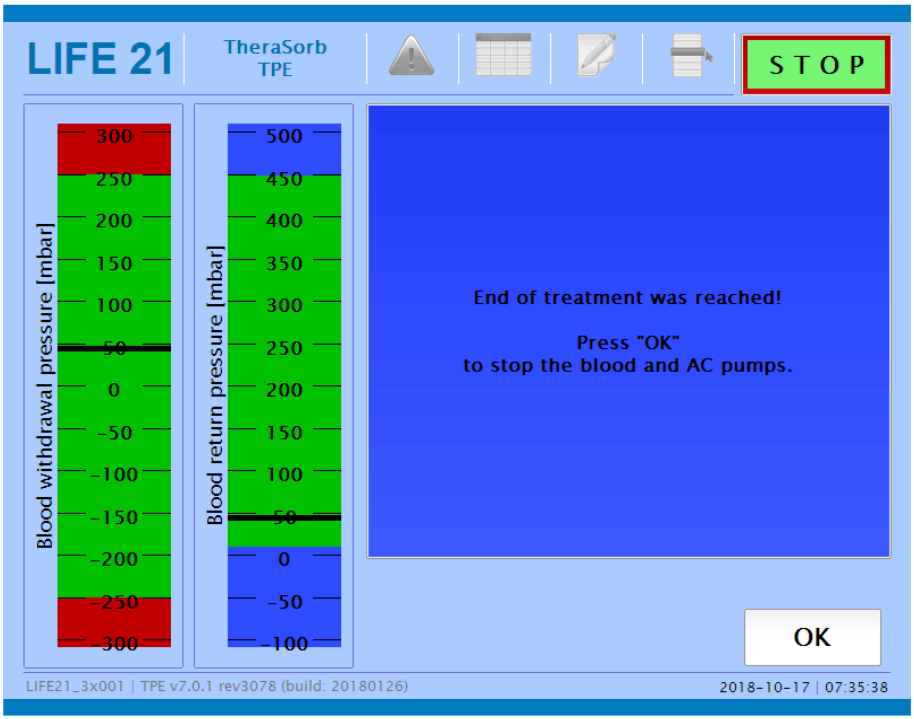
As soon as the previously defined plasma exchange volume has been reached, the plasma separation will be stopped and the blood flow will be reduced to 10 mL/min. Blood is withdrawn from and returned to the patient at this blood flow to avoid coagulation in the extracorporeal circuit. The automated reinfusion phase will be started and is divided into the following steps:

- Return of blood from single needle chambers (only single needle mode)
- Return of blood from blood withdrawal line
- Return of blood/plasma from disk separator, and return of plasma to patient
- Disconnection of patient

8.1 Reinfusion

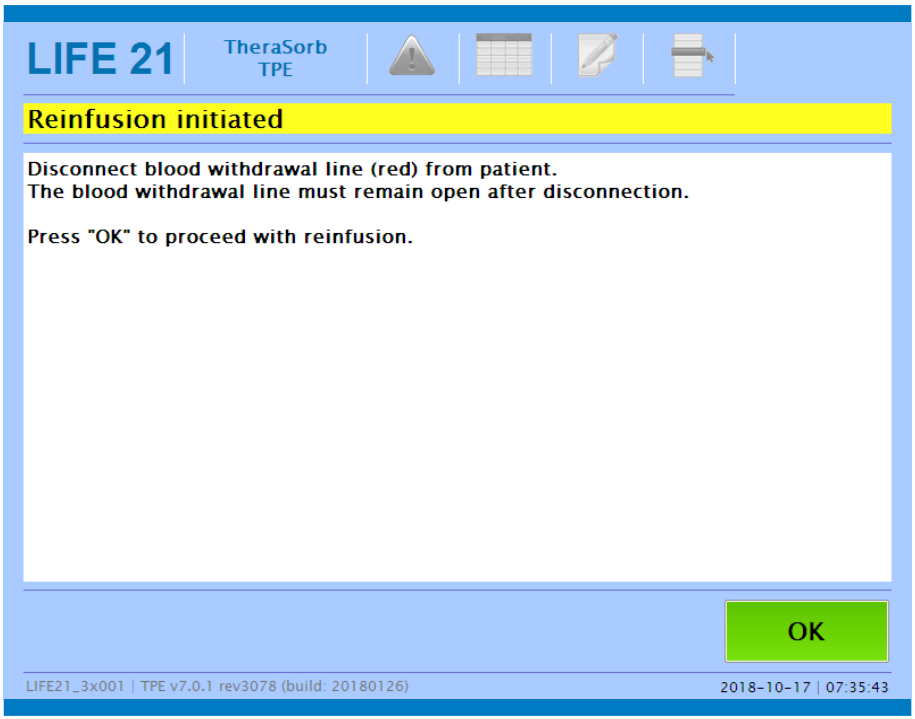
Before the reinfusion can be started the operator is informed that the end of the treatment was reached (Screen 8.1).

Operator action: Press **OK** on screen to stop the blood pumps.



Screen 8.1: End of treatment

Operator action: Follow the instructions on the screen (Screen 8.2). In the double needle mode the reinfusion starts by emptying the blood withdrawal line. In the single needle mode the single needle chambers will be emptied first. The blood withdrawal line has to remain open after disconnection from the patient to enable emptying of that line.

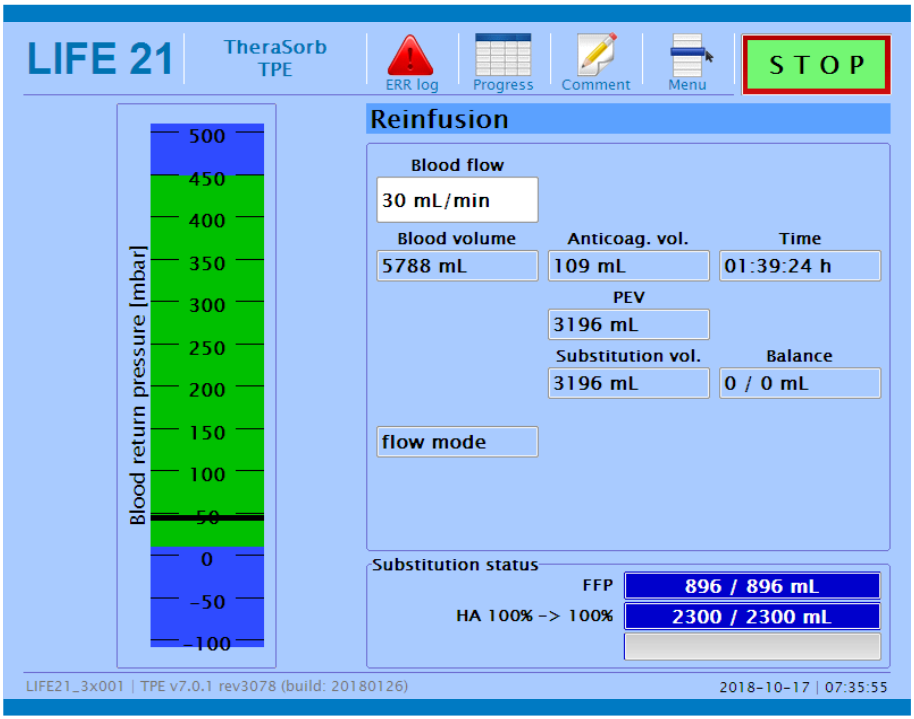


Screen 8.2: Disconnection of patient

⚠ CAUTION

Observe adequate hygienic measures for aseptic handling to prevent contamination of the fluid path during emptying of the blood withdrawal line.

Operator action: After pressing **OK** the reinfusion of the remaining blood and plasma back to the patient is started with a flow of 30 mL/min. The reinfusion screen will be displayed (Screen 8.3). A summary and explanation of each element displayed on the reinfusion screen can be found in Table 8.1. The reinfusion status is displayed continuously on the reinfusion screen and the remaining time is shown (Screen 8.4).

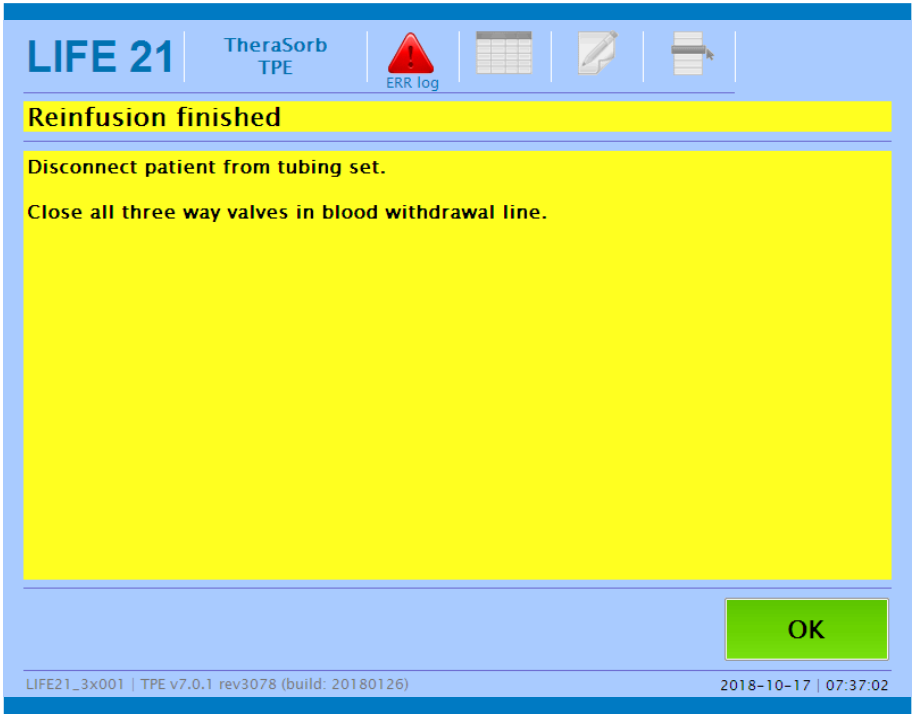


Screen 8.3: Representative reinfusion screen

Display element	Function
STOP	Interrupts the reinfusion temporarily. All pumps are stopped.
Restart	Continues a temporarily interrupted treatment.
Pressure bar	Displays blood return pressure in blue. The tolerance limits can be manually adjusted.
Blood flow	Gives access to modify the reinfusion flow rate.
Status information:	
Time	Time of treatment (elapsed)
Reinfusion balance	Course of the balance during reinfusion
Balance	Current total balance situation
Yellow status line	If the yellow status line is displayed, additional hints are given or an operator action is required.

Table 8.1: Function of elements displayed on reinfusion screen

Operator action: Follow the instruction on screen (Screen 8.4) and press **OK**.

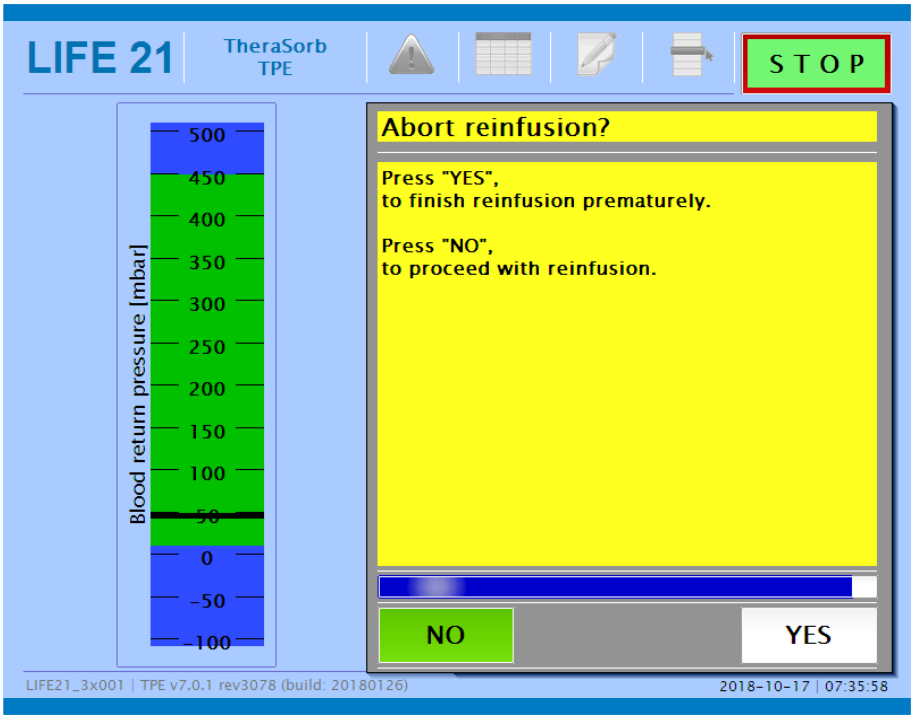


Screen 8.4: Disconnect patient from the system

8.2 Cancellation of reinfusion

The reinfusion phase can be ended prematurely if needed.

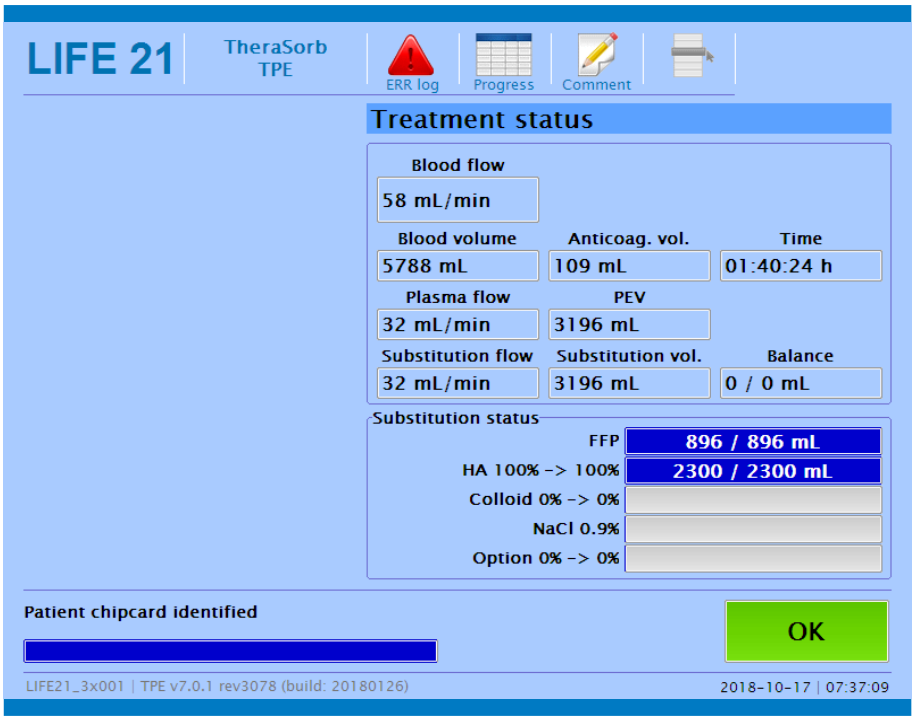
Operator action: Press **Menu** and **Abort reinfusion** on reinfusion screen. A screen (Screen 8.5) is displayed to confirm the selection. Afterwards the operator is instructed to disconnect the patient from the tubing set (Screen 8.4). Continue with chapter 8.3.



Screen 8.5: Cancellation of reinfusion phase

8.3 Treatment overview and options

After the end of the reinfusion phase and the disconnection of the patient a summary screen (Screen 8.6) is shown, allowing the operator to enter additional information.

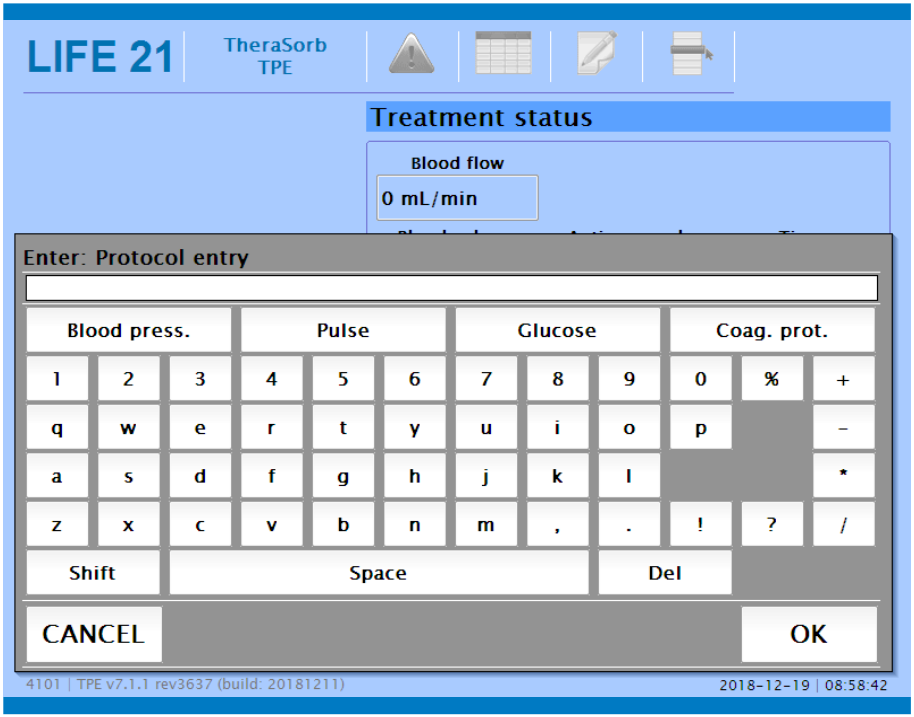


Screen 8.6: Treatment status screen

Before pressing **OK** the operator has the following options:

8.3.1 Entry of additional information for a treatment protocol

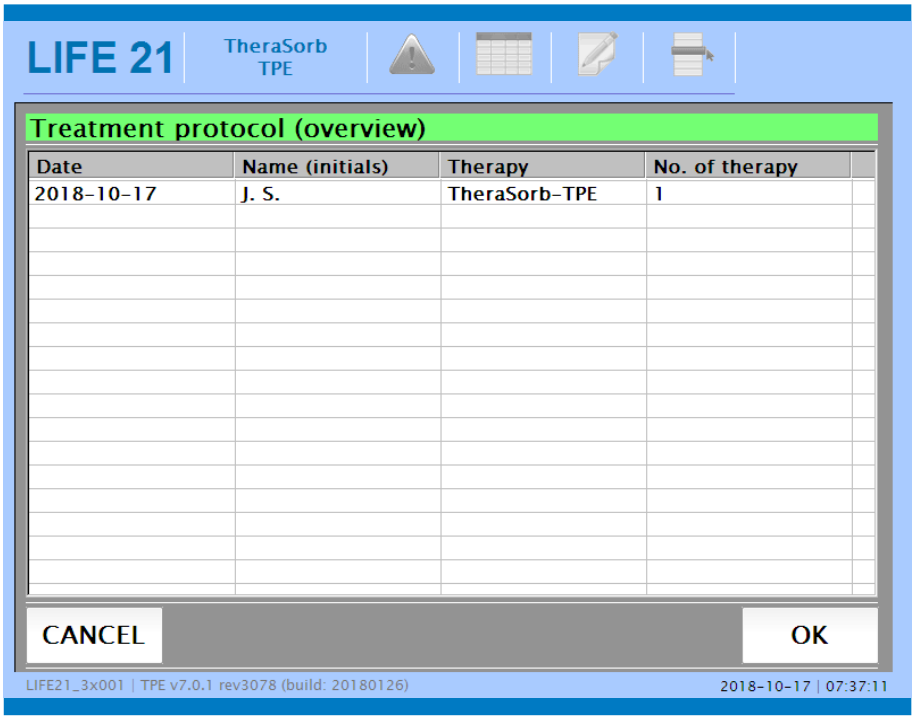
Operator action: Press **COMMENT** to enter additional information related to the treatment or patient (Screen 8.7).



Screen 8.7: Entry of additional information

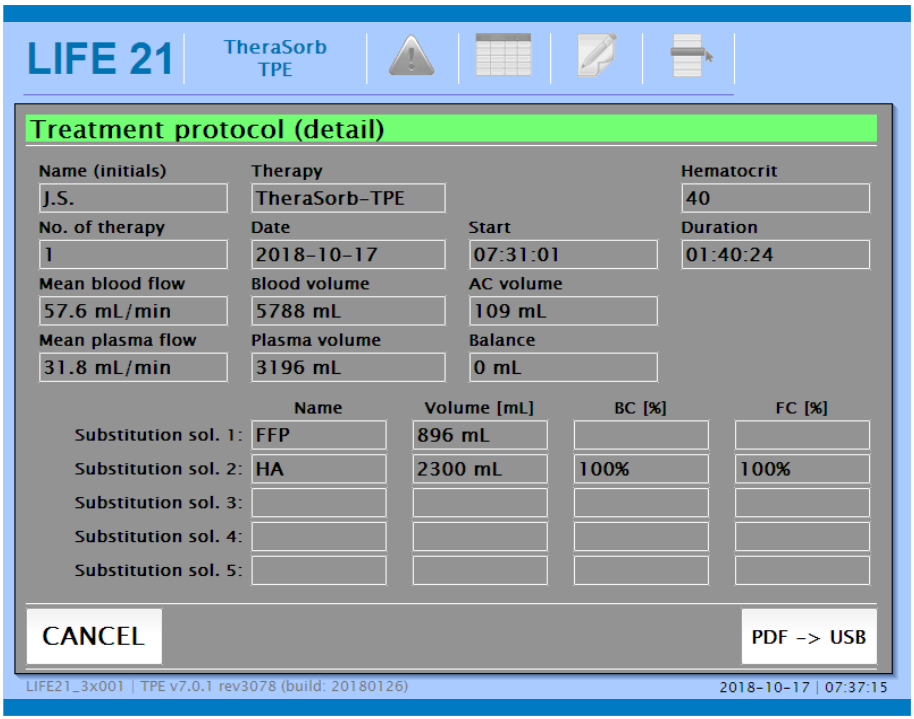
8.3.2 Transfer of treatment protocol to USB stick

Operator action: The treatment protocol can be accessed by pressing **PROGRESS** on the menu bar.



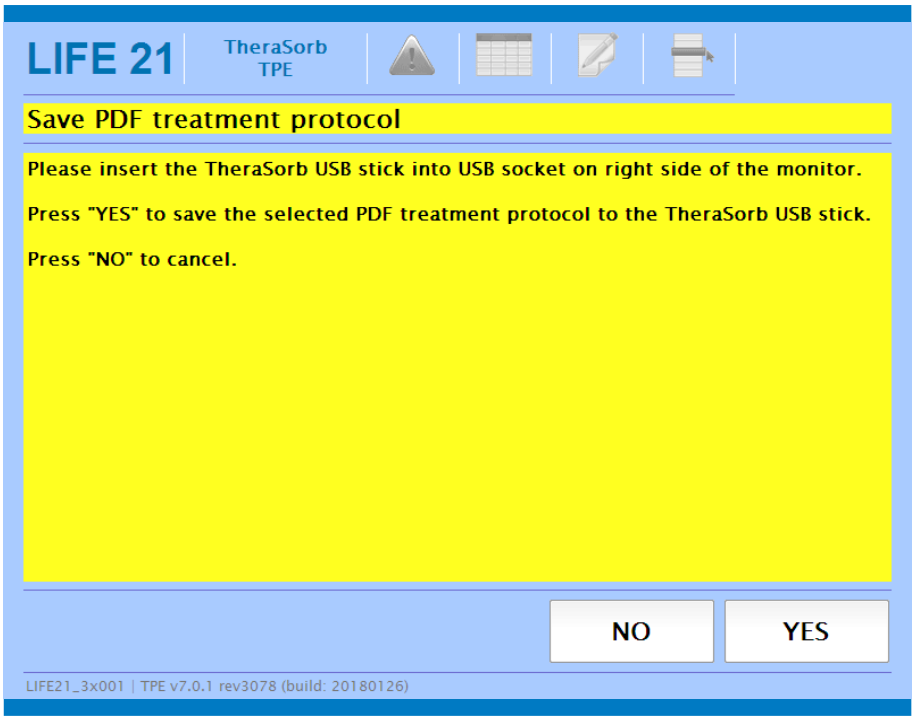
Screen 8.8: Treatment protocol (overview)

Operator action: After selecting the relevant treatment protocol press **OK** and the specific treatment summary screen is shown (Screen 8.9).



Screen 8.9: Treatment protocol (detail)

Operator action: Press PDF -> USB and follow the instructions to transfer the treatment protocol to the USB stick (Screen 8.10).



Screen 8.10: Treatment protocol (detail)

Operator action: After transferring the protocol the treatment status screen is shown (Screen 8.6). Press OK and continue with chapter 8.4.

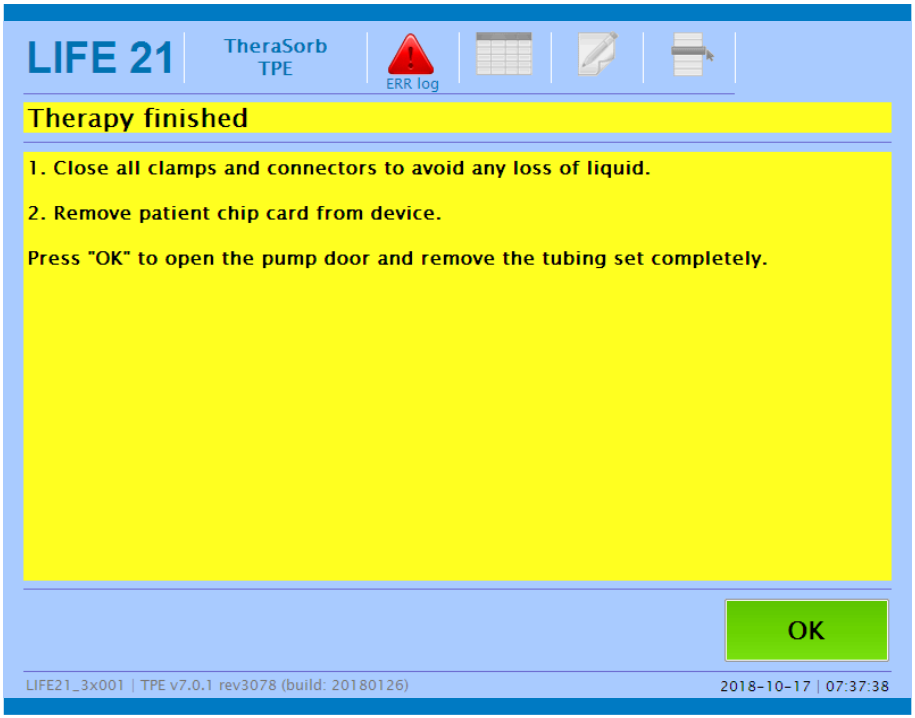
8.4 Shut down

Operator action: To end the treatment and to shut down the device follow the instructions on the screens (Screen 8.11).

- Clamp off all solution lines, patient line, and waste line
- Remove all bags
- Remove tubing lines from external pressure sensors with hydrophobic filters
- Open pump door by pressing **OK** and remove pump cassette
- Remove disk separator from separator drive
- Close pump door
- Press **OK** button to shut down the system (Screen 8.12)
- Turn off apheresis unit when prompted
- Remove patient chip card

⚠ CAUTION

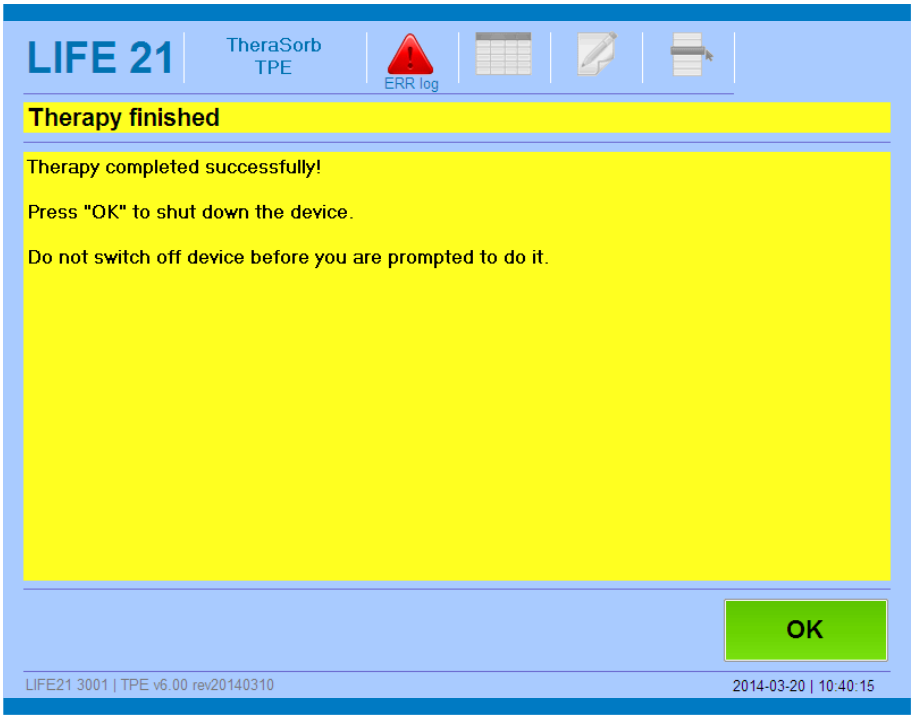
All materials, which have been in contact with blood or plasma must be treated and disposed as biohazardous materials according to standard hospital or institutional requirements and national legislations.



Screen 8.11: Representative screen on shut down instructions

IMPORTANT

If the treatment protocol has not been saved to a USB stick (see chapter 8.3.2) there are two options to save the protocol instead. The protocol can be transferred to a USB stick by using the History button on the therapy selection screen at the beginning of a new treatment. Or, the protocol can be saved from the patient chip card before beginning the next treatment. The data on the patient chip card will be overwritten during the subsequent treatment session.



Screen 8.12: Representative screen to with instructions to shut down the device

9

Permissible ranges of treatment parameters

A summary of all permissible ranges and values is shown in Table 9.1.

Parameter	P, T, R[1]	Limits (Default setting)	Unit
Last Name	P	up to 30 characters	–
First name	P	up to 30 characters	–
Date of birth	P	DD.MM.YYYY	–
Hematocrit	P	25 to 55	%
Height	P	<255	cm
Weight	P	<350	kg
Gender	P	Male (M) or female (W)	–
Blood withdrawal flow SN DN	P, T	 10 to 120 (30) 5 to 120 (30)	mL/min
Anticoagulation flow:	P, T		
ACD-A		0; 2.5 to 10 or 1:40 to 1:10 (1:18 resp. 5.5%)	% Volume parts
Heparin		0; 30 to 300	mL/h
PEV	P	≤10% BW (body weight)	mL
Balance	P	–10% to +10% PEV	mL
Volume S1:HA	P	≤100% PEV + balance	mL
Volume S2:FFP	P	≤100% PEV + balance	mL
Volume S3:Colloid	P	≤1.5% BW (body weight)	mL
Volume S4:NaCl	P	≤2.8% BW (body weight)	mL
Volume S5: Optional	P	≤100% PEV + balance	mL
Base concentration	P	1–100	%
End concentration	P	1–100	%

Parameter	P, T, R[1]	Limits (Default setting)	Unit
Bag vol S1–S5*	P, T	100 to 5000	mL
Waste bag volume*		10000 = standard bag, central = connection to central waste system or ??? = free input of bag volume, range 100…10000	mL
Name S5	P	up to 10 characters	
Standby-flow	T	10	mL/min
AC-bag volume*	P, T	100 to 5000	mL
Blood withdrawal pressure	T	–188 to +188 –250 to +250	mmHg mbar
Blood return pressure	T, R	+8 to +338 (SingleNeedle: –188 to +338) +10 to +450 (SingleNeedle: –250 to +450)	mmHg mbar
Comment	T, R	< 80 characters	
Reinfusion blood flow	R	5 to 120 (30)	mL/min

Table 9.1: Standard values and limits for the process; P = Preparation, T = Treatment, R = Reinfusion;
* = Volume for monitoring the bag volume and alert

10 Troubleshooting

For troubleshooting issues regarding the LIFE 21 apheresis unit refer to the LIFE 21 apheresis unit user manual “General Instructions and troubleshooting”.

If an error cannot be overcome by countermeasures described in the LIFE 21 apheresis unit user manual, inform the Technical Support. Note the error number on the screen for easier identification of the problem.

For filing a complaint submit the customer complaint form with all pertinent information.

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11 Legal notices

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Should the LIFE 21 apheresis unit be used in a manner not explicitly described in this manual, all warranties will be null and void.

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