SERVATOR H SALF
STERILE PYROGEN-FREE SOLUTION FOR ORGANS PERFUSION AND FLUSHING
NOT FOR DIRECT INJECTION OR INTRAVENOUS INFUSION

COMPOSITION: 1000 ml solution contains:
- sodium chloride 0.8766 g 15.0 mMol
- potassium chloride 0.6710 g 9.0 mMol
- magnesium chloride · 6 H₂O 0.8132 g 4.0 mMol
- histidine hydrochloride · H₂O 3.7733 g 18.0 mMol
- histidine 27.9289 g 180.0 mMol
- tryptophan 0.4085 g 2.0 mMol
- mannitol 5.4651 g 30.0 mMol
- calcium chloride · 2 H₂O 0.0022 g 0.015 mMol
- potassium hydrogen 2-oxopentandioate 0.1842 g 1.0 mMol

OTHER INGREDIENTS
- Potassium hydroxide 2N to pH adjustment q.s.
- Sterile Water for injection q.s.

Physical properties: pH: 7.02 - 7.20 at 25°C (77°F); pH: 7.40 - 7.45 at 4°C (39.2°F)
Osmolality: 310 mOsm/Kg

CAUTION: Federal law restricts sale of this device to, or on the order of, a physician or licensed practitioner.

INDICATIONS FOR USE: The SERVATOR H SALF solution is indicated for perfusion and flushing donor kidneys, liver, pancreas, and heart prior to removal from the donor or immediately after removal from the donor. The solution is left in the organ vasculature during hypothermic storage and transportation (not for continuous perfusion) to the recipient.

WARNINGS AND PRECAUTIONS:
- **Warning:** Perfusion of the kidney, liver and/or heart should be carried out with a maximum hydrostatic pressure of 120 mm Hg.
- **Warning:** SERVATOR H SALF is not indicated for intravenous or intraarterial administration. It is indicated only for selective perfusion of the kidney, liver and heart and for cooling of the surface areas, i.e., for the preservation of the donor organ during the transport from donor to recipient. SERVATOR H SALF may not be used for systemic infusion.
- **Warning:** SERVATOR H SALF is not indicated for continuous perfusion.
- **Warning:** Keep out of reach of children.
- **Caution:** The product must be used before the expiration date stated on the package.
- **Caution:** Use the solution only if clear and without visible particles.
- **Caution:** The product must be stored according to the recommendations prior to use.
- **Caution:** Discard any residue to avoid risk of contamination due to loss of sterility.
- **Caution:** The solution is sterile and is intended for one single and continuous administration
- **Caution:** Unused residues of the solution should be disposed of in conformity with the local rules in force.

ADVERSE EVENT: No side effects have been encountered that could be attributed to this product.

INTERACTION WITH OTHER MEDICAL PRODUCTS: Interactions with such therapeutic agents as glycosides, diuretics, nitrates, antihypertensives, beta blockers and calcium antagonists, which are used perioperatively, have not been reported. The SERVATOR H SALF solution must not be mixed with other drugs.
OVERDOSES (SYMPTOMS, COUNTERMEASURES)
In the case of entry of the SERVATOR H SALF solution into the general circulation, the resultant change in the concentration of sodium and calcium is very slight.
After checking sodium and calcium levels in the extracorporeal circulation both of these electrolytes should be replaced if necessary.

INSTRUCTIONS FOR USE (RECOMMENDATIONS)
Required Equipment:
- Perfusion apparatus with a Y-piece for bottle or bags;
- Perfusion cannula tube 2.5 to 3 mm;
- Tube clamp;
- Perfusion stand with a height setting of up to 200 cm with tape measure.
Cooling Equipment (5 to 8° C) for use in cardiac surgery;
- Perfusion tube with an internal diameter of 6 mm;
- Transport Container with sterile pouch for transport of the cooled organ from donor to recipient.
Filtration of SERVATOR H SALF is not necessary or recommended.

TOLERANCE OF ISCHEMIA BY THE KIDNEY
The kidney may be stored with ice cold SERVATOR H SALF solution at about 2 to 4°C with a period of (cold) ischemia of up to 48 hours.
Warm ischemia time, that is to say the average time period required for the completion of anastomosis of the vessels, is usually 30 minutes.
Taking this time as a basis, the organ recovers completely with optimal immediate function within 24 hours.

TOLERANCE OF ISCHEMIA BY THE LIVER
The liver may be stored with ice cold SERVATOR H SALF solution at about 2 to 4°C with a period of (cold) ischemia of up to 15 hours.
Warm ischemia time, that is to say the average time period required for the completion of anastomosis of the vessels, is usually 30 minutes.
Taking this time as a basis, the organ recovers completely with optimal immediate function within 24 hours.

TOLERANCE OF ISCHEMIA BY THE HEART
The Heart may be stored with ice cold SERVATOR H SALF solution at about 2 to 4°C with a period of (cold) ischemia of up to 4 hours.
Warm ischemia time, that is to say the average time period required for the completion of anastomosis of the vessels, is usually 30 minutes.

INTRODUCTION OF RENAL PERFUSION
Following successful laparotomy, the kidney is prepared by ligature of the capsular vessels. The perfusion catheter for selective kidney perfusion is fixed in the renal artery using a tourniquet.
Cold perfusion (2-4°C) is performed under hydrostatic pressure (maximum of 120 mmHg). Within the first minute of perfusion, the renal vein is incised and clamped off adjacent to the vena cava.
The escaping perfusate is removed from the abdominal cavity. After approximately 10 minutes of perfusion, the kidney is resected before transplantation.

INTRODUCTION OF HEPATIC PERFUSION
The donor should be heparinised appropriately, and the aorta or the iliac bifurcation and the portal vein will be exposed.
The perfusion tubing should be of the largest possible diameter and the cannulae should have an internal bore of at least 5 mm.
Because of the low viscosity of the solution, perfusion is performed under hydrostatic pressure only (maximum of 120 mmHg).
Perfusion of the portal vein can be performed by cannulating the superior or inferior mesenteric vein and advancing the catheter up to the origin of the portal vein.
After performing cannulation, clamping off the aorta and opening the vena cava, bubble-free perfusion is begun via both lines simultaneously.
As a general rule, 8-12 liters of HTK at 2-4°C should be perfused (about 300 ml per kg of body weight) and this will require about 10 minutes.
Should the center decide to use the so-called aorto-single flush technique, the total amount of the preservation solution needed is perfused only via the aortal line.
Once again, a pressurized infusion is not necessary or recommended. A Y-perfusion system is recommended in addition to perfusion tubing of the largest possible caliber and perfusion cannulae with an internal bore of at least Charrière 15 (5 mm). The time required for perfusion is extended by about 5 minutes.

At the implant site, the back-table preparation includes the reperfusion of approximately 500 ml cold HTK solution.

The perfusion is stopped when the anastomoses of the inferior vena cava are completed at the end of the second warm ischemia time.

It is permissible, in view of the flow properties and low potassium concentration of the HTK solution, to perform flushing of the organ or testing for leaks in the anastomoses with HTK solution itself, if necessary. Alternatively, any standard flushing solution may be used. Simultaneous reperfusion via the artery and the portal vein are preferable, though primary reperfusion through the portal vein alone is acceptable.

**INTRODUCTION OF CARDIAC PERFUSION**

The inactivation of the heart renders it susceptible to overstretching. Decompression of the left ventricle must therefore be performed at the commencement of cardioplegia.

For adult hearts the following recommendation is appropriate: The solution, cooled to 5°C-8°C, is perfused into the coronary arteries by hydrostatic pressure of 100 mmHg (equivalent to initial height of perfusion bottle above level of heart = 140 cm). After cardiac arrest has ensued (within the first minute after starting perfusion) the perfusion bottle should be lowered to about 50-70 cm above the level of the heart, equivalent to 40-50 mmHg. In patients with pronounced coronary stenosis, a higher perfusion pressure (about 50 mmHg) will be necessary for a somewhat longer time.

The overall perfusion time should be 6-8 minutes, so as to ensure homogeneous equilibration. Even for small hearts, a perfusion rate of 1 ml/min/gram-estimated-heart-weight at a perfusion pressure of 40-50 mmHg and a perfusion time of 6-8 min should be enough to ensure equilibration.

The heart may then be excised. The heart should tolerate a cold ischemic time of up to four hours.

**TRANSPORT OF A DONOR ORGAN**

The transport of a donor organ to the recipient utilizes a sterile pouch accommodating the size of the organ in an ice cold SERVATOR H SALF solution.

The organ must be completely covered by the solution. The pouch is sealed with adhesive tape and is placed into a second container which is also filled with SERVATOR H SALF solution in order to prevent a breakdown of insulation and cooling by trapped air. The double-bagged organ is placed into a sterile plastic container and closed with a secure lid.

The plastic bag is then placed into a transport container packed with ice for transport. Information about the donor, copies of the laboratory results and blood samples from the donor are also included.

The transport of the donor organ in SERVATOR H SALF solution must be accomplished as quickly as possible.

**ADVERSE EVENTS OBSERVED IN THE CLINICAL STUDIES PERFORMED WITH SIMILAR PRODUCT**

**KIDNEY STUDIES**

There were no unexpected adverse events in these clinical studies. The adverse events that occurred were expected because of the nature of transplantation. None are believed to be affected by any of the solutions.

Kidney failure rates in the first 48 hours were comparable in all groups: UW-15/297 and HTK-18/314; EC-15/277 and HTK-13/272.

In the HTK-UW kidney study, acute rejection episodes occurred in 99/314 (32%) in the HTK group and 105/297 (35%) in the UW group. In the HTK-EC study, acute rejection episodes occurred in 99/292 (34%) in the HTK group and 108/277 (39%) in the EC group.

**LIVER STUDIES**

There were no unexpected adverse events in these clinical studies. The adverse events that occurred were expected because of the nature of transplantation.

In the multi-center trial, primary disfunction rate (PDF) was 10.3%, with a primary non-function rate (PNF) of
3.6%. Bile duct complications were seen in 19% of transplants. This compares with data from Eurotransplant on the UW solution: PDR of 15.2% and PNR of 7.8%.

**HEART STUDIES**
There were no unexpected adverse events in these clinical studies. The adverse events that occurred were expected because of the nature of heart transplantation.

In the Bad Oeynhausen experience, the primary dysfunction rate (PNF) was 1.9%.

**STORAGE CONDITIONS:** Store in refrigerator (+2°C to +15°C; 35°F / 59°F) and protect from light.

**HOW SUPPLIED:** PVC-free bag 1000 ml  
PVC-free bag 2000 ml.

**MANUFACTURER:** S.A.L.F. S.p.A. LABORATORIO FARMACOLOGICO  
via Marconi, 2 - 24069 Cenate Sotto (BG) Italy

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<th>SYMBOLS USED ON THE PRIMARY PACKAGING AND BOX LABELS</th>
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