Guidelines for anaesthetic organ protection during organ procurement from adult donation after brain death (DBD) donors

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CNDO Nationaler Ausschuss für Organspende Comité National du don d'organes

Autorenteam: Dr Christian Brunner MD, Dr Olivier Huot MD, PD Andreas Vogt MD

Expertenteam:

Dr Raphaël Giraud MD, PD Franz Immer MD, Dr Nathalie Krügel MD, Dr Mathias Nebiker MD

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Introduction

Worldwide 715,482 patients have received a lifesaving organ transplant since 1988, and in 2016, in the USA alone 33,600 transplants were performed [1]. According to the 2019 Eurotransplant Annual Report, a total of 13,968 patients were on the waiting list at the end of 2019 [2]. In the USA, the number of patients on the waiting list was 23,198 at the end of 1991, increasing to 112,568 patients in 2019 [2]. The shortage of organs is aggravated by the growing discrepancy between the number of donors and transplants and the size of the waiting list. Optimal donor management could improve the availability and quality of donor organs [1].

During surgery for organ removal, all anaesthetic measures are aimed at both optimal organ and tissue perfusion and at protecting the organs.

Anaesthetic management can primarily be regarded as an extension of the intensive medical organ preservation measures [1, 3]. Analgesia and unconsciousness are not an anaesthetic requirement during organ removal [4].

Protocol-based intensive care measures immediately following the determination of brain death seem to increase the quality and quantity of organs available [5].

Continuing the intensive care, organ-preserving therapy of a donor in the operating theatre is a great responsibility and must be conducted by an anaesthesiology team with the appropriate experience in multi-organ procurement (MOP) [6-9].

It is the responsibility of anaesthesiologists and anaesthesiology nursing staff in the operating theatre. Anaesthetic treatment in the operating theatre was long considered unnecessary due to the brain death of the donor and the de facto lack of benefit to donors. The experience of the removal teams and common practice has shown the opposite, however, and publications in this direction can also be found in the specialist literature [7 - 9; 10]. Both scientific societies and organ transplant organizations have issued very clear recommendations and guidelines in this context (Swiss Donation Pathway, National Health Service Blood and Transplant etc.)

Method

This paper aims to support specialist medical personnel in making decisions on the treatment of patients with irreversible brain damage who are organ donors. However, it cannot replace a clinical evaluation.

The detailed document analysis is mainly based on publications available in PubMed and the recommendations of North and South American organ transplant organizations and European organizations (in France, Switzerland, the United Kingdom, Spain etc.).

The sources were reviewed by an editorial committee comprising doctors from the National Committee for Organ Donation (CNDO), the Swiss Association of Anaesthesiologists and Swisstransplant.

Given the subject matter covered in this document, laws, draft laws, decrees, ordinances and resolutions were also consulted as sources. The same applies for recommendations from organisations, foundations and international associations.

The references were critically assessed and classified into three levels of evidence according to the strength of the evidence and the recommendations formulated, as is customary when recommendations are prepared by European and international scientific societies.

Different levels of evidence and recommendations may be applied here. Two of them are used in the present work:

- The first level of evidence was published and is applied in Switzerland [11], although its application is rather complicated.
- The second comes from frequently used North American recommendations [6] and is
 presented in the following table, which is mainly based on an evaluation of recent studies.

Type of recommendation	Application modalities for Swisstransplant	Markings in the text
Strong consensus	Must be applied during treatment	+++
Weak consensus	Action is strongly recommended	++
No or little consensus	Lack of reason: decision of the team	+

If not marked with [®], medications used are listed with their international non-proprietary name.

1.0 Preoperative measures

After brain death has been determined and after notification by the organ procurement coordinator, premedication is administered in the intensive care unit.

The following information for premedication must be made available by the intensive care unit and the transplant coordination team for anaesthesiology documentation:

- Medical and surgical history: allergies and cardiovascular disorders that may influence organ preservation treatment
- 2. Mode of ventilation and possible ventilation difficulties
- 3. The haemodynamic condition of the patient and the vasoactive agents required to maintain organ perfusion
- 4. Up-to-date laboratory results
- 5. Available or required blood products (red cell concentrate, fresh frozen plasma, platelets)
- 6. Times at which various medication must be administered (antibiotics, corticoids etc.)
- 7. Already identified complications and / or organ failure (dysrhythmias, dyscrasias etc.)
- 8. Existence of a death certificate duly completed and signed by the persons involved
- 9. Procurement modalities (number of teams, organs to be removed, tissue to be removed, times etc.)
- 10. Already initiated or planned monitoring

1.1. Transfer from the intensive care unit to the operating theatre

- 1. Reduce monitoring to a minimum
- 2. Have blood group card ready and ensure that blood products are available, prescriptions as necessary
- 3. Maintain protective ventilation to ensure that tissue and lungs are adequately oxygenated in case of procurement
- 4. Have the full medical history at hand
- 5. Minimize the risk of allergies (especially latex allergy) of donors and especially of organ recipients

Recommended monitoring and medication to be prepared before transfer to the operating theatre:

- Electrocardiogram (ECG) 5 leads
- End-tidal carbon dioxide (EtCO₂)
- Pulse oximetry oxygen saturation (SpO₂)
- Arterial catheter
- Central venous pressure (CVP)/central venous oxygen saturation (ScvO₂)
- Pulmonary artery pressure / pulmonary artery occlusion pressure / cardiac output (CO) / mixed venous oxygen saturation (SvO₂) (if Swan-Ganz catheter required)
- Measure CO (CardioQ®, Flowtrac®, ProAct®, PiCCO® etc.) (optional)
- Transoesophageal echocardiography

- Temperature
- Urine flow
- Gastric tube and tube for lung surgery

Absolutely essential medications (+++):

- Non-depolarising curare
- Morphinomimetics (morphine, fentanyl, sufentanil ++)
- Volatile anaesthetic (sevoflurane ++), halothane and derivates
- Vasoactive amines (noradrenaline, adrenaline, isoprenaline, dobutamine)
- Atropine ineffective in brain death patients (++); if necessary, prefer isoprenaline
- Medications to lower blood pressure (nitro derivatives, sodium nitroprusside, alpha-1-blocker, urapidil (Mediatensyl®, Eupressyl®, Ebrantil®)
- Beta-blocker with short half-life (esmolol)
- Lidocaine
- Electrolyte solutions (calcium, magnesium, potassium)
- Heparin sodium (300 UI/kg), to be used after surgical examination of large arterial and venous vessels
- Amiodarone

Supplementary medication (++)

- Diuretics (furosemide)
- Antibiotics, depending on clinical findings and organs to be removed
- Corticosteroids: hydrocortisone (methylprednisolone for lung removal)
- Desmopressin (Minirin®) / arginine vasopressin) (Empressin®)
- Other medications (amiodarone) as required

Other material:

- Ventilator suitable for the patient (standard or extra powerful) with filter
- System for administering inhalational anaesthetics
- Device for warming the infusions and a warming mattress
- Defibrillator, at hand
- Infusion solutions, preferably crystalloid solutions
- Red cell concentrate (leucocyte depleted), plasma (fresh frozen plasma) and, if necessary, platelet concentrate, if necessary, prothrombin complex concentrate (prothrombin complex, concentrate factor II – prothrombin – VII – proconvertin – IX – antihaemophilic factor B and X – Stuart factor) (Prothromplex[®])

2.0 Anaesthetic organ protection during multiple organ removal

2.1. Preparation of the patient in the operating theatre

Check preparation: Depending on the type of procurement intended and the necessity to preserve the haemodynamics, check the following:

- 1. Correct positioning
- 2. 2 functional peripheral venous lines of appropriate size
- 3. Device for warming infusions
- 4. Positioning the pulse oximeter
- 5. Intubation tube and gastric tube in position

When preparation is complete, a blood gas analysis must or may be performed. This will demonstrate that the following clinical targets are being met, thus ensuring adequate organ perfusion. These targets are defined as follows (+++)[12-15]:

- 1. Mean arterial pressure (MAP) between 60 and 70 mmHg
- 2. Systolic blood pressure >100 mmHg
- 3. Heart rate (HR) 60 120 bpm
- 4. Diuresis between 0.5 and 4 ml/kg/hrs
- 5. Warm periphery
- 6. Duration of skin discolouration after pressure <2 s (paediatrics)
- 7. SvO₂ >65% or ScvO₂ >70%
- 8. Core body temperature within the target values
- 9. Haemoglobin >70 g / l

During multi-organ procurement (MOP), specific haemodynamic issues associated with brain death may occur. These are discussed in the following sections.

2.2. Hypotension

- 1. Exclusion of septic or obstructive shock such as pulmonary embolism, pneumothorax, tamponade
- 2. Compensate or prevent the volume deficit (brain damage) associated with vasoplegia by means of crystalloids, if necessary, with gelatine preparations, fresh plasma and/or albumin.
 - For hypovolaemia (pulse pressure variation (PPV) >13%, CVP <8 mmHg/pulmonary artery occlusion pressure <10 mmHg/δ TA >10%)
 - —> Crystalloids, 500 ml, repeat over 15 20 min (2nd option: colloids, except for lung removal)

- For Hb <70 g/l transfusion of leucocyte depleted red cell concentrate (after taking blood for HLA and AB0 typing, 2nd typing)</p>
- For heart failure (limbs marbled and pale, cardiac index <2.21/m² ↓, CO measured
 <1.51/min ↓, SvO₂ <65%, ScvO₂ <70%)
 - → Dobutamine ≤ 5µg/kg/min, then Empressin®, because of its effect on the volume maintenance, then adrenaline, if necessary, noradrenaline according to the respective protocol
 - \longrightarrow If necessary thyroid hormone T₃, if not already administered as a continuous i.v. infusion from the onset of brain death
- If points 1 and 2 have been excluded or treated, it is likely to be a distributive shock.
 → Noradrenaline in increments: 0.05 µg/kg/min, then 0.5 1µg/kg/min up to finally max 2 3µg/kg/min
- For suspected diabetes insipidus:
 - Treatment with Minirin[®]: 1 4 µg direct i.v., repeat every 4 8 hours depending on diuresis
- Also consider:
 - —> 50 mg hydrocortisone every 6 hours, if not already administered in the intensive care unit
 - Additional volume administration in any case; at the same time electrolyte imbalances and the temperature must be corrected as far as possible

2.3. Hypertension

Medications to lower blood pressure with a short half-life (nitro derivatives, sodium nitroprusside) are used to treat rapid pressure reduction in brain-dead patients. In the operating theatre, inhalation anaesthetics such as fluranes and opiates can be used.

2.4. Bradycardia

3 causes:

- 1. Acute hypovolaemia (mobilisation, positioning, haemorrhage etc.)
- In children, dominant parasympathetic activity has been observed as a result of decreasing sympathetic activity (brain death)
- 3. Reflex vagal stimulation of the mesentery, vessels and joints during incision or traction [17] Prevention: Use of opiates with peripheral effects [18 20].

Brain-dead patients respond poorly to atropine, except for parasympathetic stimulation (+) [21].

If this is the case, therapies of choice are: Isoprenalin (Isuprel[®]): bolus i.v.: $10 \mu g$, repeat if necessary, then infusion: i.v. $0.02 - 0.5 \mu g/kg/min$ and/or ephedrine.

Then positive chronotropic medication:

MAP between 60 and 90 mmHg: Dobutamine $\leq 5 \,\mu g/kg/min$ MAP <60 mmHg: Adrenalin 0.02 - 0.15 $\mu g/kg/min$

There is a risk of arrhythmias, especially in case of electrolyte imbalance. For all patients: External or possibly transjugular pacing.

2.5. Other arrhythmias

Remember to correct electrolyte imbalances.

Especially for calcium: Ca++ = 2.3 - 2.54 mEq/l(1.15 - 1.27 mmol/l), requires treatment from 2.1 mEq/l(1.1 mmol/l) [10].

Magnesium 4 g (16 mmol), slow i.v. over 15 min

Defibrillation can be performed using guidelines established in the facility.

Antiarrhythmic agents: Medications with a short half-life are preferable. In the presence of coronary artery disease and/or altered left ventricular function for the treatment of supraventricular tachycardia, or if there is slowed or reduced atrial fibrillation or atrial flutter, **amiodarone** can be used.

2.6. Coagulation disorders

Coagulation disorders are not uncommon in brain-dead patients, their aetiology is often multifactorial (haemorrhage, hypothermia, haemodilution). Coagulation tests in routine diagnostics are rather unspecific and often not very helpful to explain the aetiology of the coagulation disorders in detail. In addition, the dead brain tissue causes patients to experience an "inflammatory storm" (before loss of cerebral blood flow), and the excessive consumption of coagulation factors and platelets leads to consumption coagulopathy, after which the disseminated intravascular coagulation continues independently. This is where symptom therapy is applied, in which the cell damage of such organs is corrected, the spent labile coagulation factors are replaced and, if necessary, an existing causal infection is treated.

The review of the personal and family medical history with regard to congenital haemostasis disorders should not be forgotten:

Asymptomatic anomalies of protein S, protein C and factor IV Leiden carry a high risk of thrombosis for the recipients of such organs.

It is therefore necessary to test for these anomalies and to transfuse the necessary products to prevent blood loss, thrombosis and fibrinolysis.

The objective of diagnosing such coagulation disorders is also to protect the organ recipient. The therapeutic objectives are:

- 1. Restoration of the deficient factor level to at least over 30%
- 2. International normalised ratio (INR) <2.0
- 3. Platelets >20,000 Giga/I (>50,000 Giga/I)
- 4. Recommended procedure: Exclude organs where the anomaly is related to the liver [22]

The measures to be taken are summarised in the following table (+++) [12].

3.0

Main side effects of brain death and recommended anaesthetic procedure

System/target values	Side effects of brain death	Recommendations for anaesthetic treatment
Cardiovascular system Targets: adult Blood pressure = MAP	Decrease in contractility Decrease in vessel resist- ance	Vasoactive amines Reduce volatile anaesthetics, preferably use Sevorane®
>70 - 90, Systolic blood pressure >100, HF 60 - 120 / min, SvO ₂ >65% or ScvO ₂ >70% pH value: 7.35 - 7.45 PaO ₂ >70 mmHg (++), PaCO ₂ normal Calcaemia normal, treat if	Rhythm disturbances, "rhythm storm" Reflex bradycardia	Correct electrolyte imbalances, beta, short anti- arrhythmics, beta-blockers Isuprel [®] : bolus of 10 µg, then 0.2 – 0.5 µg / kg / min, if necessary ESS? Stronger narcosis (morphine products)
(or <1.1mmol/I)	Hypovolaemia due to polyuria	Volume substitution, compensate losses Empressin®, desmopressin Transfusion red cell con- centrate (keep Hb between 60 and 80 g/l) Albumin, fresh frozen plasma

Lung Targets: protective ventila- tion: 6 – 8 ml/kg – 1 of the initial weight, PEEP 8 – 10 cm H ₂ O. FiO ₂ = 40%, plateau pressure <35 mmHg, peak pressure <40 mmHg closed suction system, infla- tion before procurement	Apnoea Atelectasis Increase of capillary permeability Pulmonary oedema	Protective ventilation Screening (chest x-ray) Restricted inflow: Analeptics, CVP monitoring between 4 and 10 mmHg Check diuresis
Endocrine system Targets: Natremia: <150 mEq/1 Normoolycaemia:	Pituitary necrosis: Diabetes insipidus Hypernatremia >150 mg/l	Desmopressin: 1 – 4 µg i.v., then ½ dose every 6 hrs or Vasopressin®, 1 bolus i.v. of 1 u, then 2.4 u/hrs
>75 to <150 mg/dl	Diabetes Hypothyroidism Adrenocortical insufficiency	Insulin infusion for blood glucose control <150 mg/dl Hormone substitution for acute phase discussed, but mainly when resuscitation lasts several days Doses Methylprednisolone i.v.: 15 mg/kg/24 hrs or 50 mg i.v. every 6 hrs Tetraiodothyronine: 20 µg bolus, then 10 µg/hrs
Haemostasis Targets: Prevent intravascular throm- bosis of the organs Prevent the transmission of congenital diseases (Leid- en-haemophilia etc.) Reduce intraoperative haemorrhage or treat haemorrhagic syndrome	Thrombophilia Consumption coagulop- athy due to the release of cytokines Dilution of the coagulation factors Dysfunction (congenital anomalies, hepatocellular insufficiency) Increased risk of thrombosis	Heparin therapy: 300 u/kg if induced, if no coagulation disorder Fresh frozen plasma, pro- thromplex: 20 to 30 u/kg If INR not available: 25 UI/kg = 1ml/kg Otherwise see dosage scheme*
Haematology Targets: Haemoglobin between 70 and 100 g / I, or haematocrit >0.30	Anaemia Hyperleukocytosis	Transfuse: Red cell con- centrate must be leucocyte depleted. Differential diagnosis infection

Musculoskeletal system	Spinal somatic reflexes, increased parasympathetic reflex action	Curarisation in the operating theatre (+++) Morphine treatment to alleviate parasympathetic reflexes
Kidneys Targets; diuresis measure- ment: 0.5 to 4 ml/hrs	Polyuria	Vasopressin: 0.01 – 0.04 u/min or Desmopressin: 1 – 4 mcg/ 6 – 8 hrs i.v./s.c.
Temperature Targets: 35 – 37°C	Thermal deregulation	Warm up if necessary (pa- tient / fluids) (+++)

* Dosing human prothrombin complex (PPSB) [23]: If INR not available: 25 UI/kg = 1ml/kg, if INR can be determined, the dosage depends on the respective agent and on the INR (Kanorad®, Confidex®, Octaplex®).

4.0

Surgical intervention

Those involved in the procedure in the operating theatre (procurement teams, anaesthesiology team, organ procurement coordinator, staff in the operating theatre) must attend a preliminary meeting before work begins, at which the aims and purpose of the procurement (clarification of who is collecting what, distribution of vessels, special needs, scientific protocols etc.) are clarified, so that each person is fully aware of the tasks of the others and can respect their work. The anaesthesiologist is often at their post and can help with the organization and coordination of the surgical work and collection of biopsies.

The teams communicate in a language that all participants are fluent in (e.g. English). Teams from abroad must respect national conditions and first consult with the local coordinator before deciding to use their equipment and solutions.

Should conflicts or discussions arise in this context, the National Transplant Coordination and/or its medical advisor must be consulted (+++).

Sequence of organ removal:

Heart – lungs – intestine – liver – pancreas (complete or islets) – kidneys Followed by tissue: cornea – bones – ossicles – cartilage – tendons

The order of operations by the surgical teams:

- 1. Abdominal surgery team (cannulation)
- 2. Heart surgery team (cannulation and procurement)
- 3. Thoracic surgery team (cannulation and procurement)
- 4. Abdominal surgery team (procurement)

The risks and complications are similar to those of other major surgical procedures: increasing haemodynamic instability due to positioning (often xipho-pubic, changes in position), hypovolaemia, one or more bleedings due to cannulation, organ dissection, hepatic dislocation, too many blood samples taken etc.

Keep eyes closed to protect cornea; use protective eye drops.

Communication with the surgical team is of utmost importance, so that everyone can adapt their behaviour to the needs of all and respect the dignity of the deceased.

The duration of the procedure at this stage is between 90 and 120 minutes. It can, however, be significantly longer if procurement is after a stroke.

This can result in considerable blood loss. It is, therefore, permissible to administer transfusions to the brain-dead patient during this removal stage to prevent prolonged reduced oxygen supply to the tissue. The target haemoglobin value is at least 70 g/l (60 to 90 g/l in some protocols).

5.0

The most important information at a glance

The use of opiates should not be prohibited.

By definition, a brain-dead patient has neither consciousness nor pain sensation. An autonomous, sympathetically mediated stress reaction with tachycardia and hypertension can affect the quality of the donor organs. Opiates can suppress this stress response and stabilize the heart rate and blood pressure (+++). Curarisation is highly recommended for the interruption of spinal reflexes to facilitate the surgical procedure (+++).

The administration of volatile anaesthetics has a protective effect against ischaemia-reperfusion injury, particularly to the heart [17 – 19]. Halogens have a positive effect on liver [24], kidneys [25] and lungs [26].

For reflex arterial hypertension, the use of fluorinated inhalation anaesthetics is indicated, but this does not address the causes.

The treatment must in no way affect the quality of the organs removed. This may be the case, for example, by the worsening of existing hypotension or by the use of halogens if the liver is hypoxic (increase in liver enzymes, mild fatty liver).

Other medications for lowering blood pressure with a short half-life (nitro derivatives, sodium nitroprusside) are used to treat rapid pressure reduction in brain-dead patients.

For simultaneous tachycardia, beta-blockers with a short half-life (esmolol/Brevibloc®) are preferred.

During lung removal, anaesthesiology measures do not end with aortic cross-clamping. The lungs continue to be ventilated until the trachea is clamped. This is done at hyperinflation so that the oxygen introduced is maintained.

Protective ventilation (+++) [8-10].

Heparin therapy with 300 UI/kg heparin must be carried out at least 2 minutes before cannulation (+++).

The red cell concentrate must be leucocyte depleted and CMV negative (for paediatric procurement or for adult organ recipients who have no immunity (50% of the Western European population under 35 years of age)) [27].

Lung removal should not be an exception, but it should be considered for every donor. There are some simple rules to follow (+++) [8, 26]:

- Restrict the supply of crystalloid fluids (e.g. use of colloids)
- The ideal tidal volume is (4 -)6 8(10) ml/kg
- Maximum plateau pressure of 35 cmH₂O
- Minimum PEEP of 5 cmH₂O and maximum PEEP of 8 cmH₂O
- FiO₂ of approx. 40%

Targets: PaO_2 : 100 mmHg (\approx 12 kPa); $PaCO_2$: 35 – 40 mmHg (4 – 5.5 kPa) If PaO_2 low: better to increase PEEP than to increase FiO_2 Methylprednisolone 15 mg/kg (Solumedrol[®]) The use of volatile anaesthetics seems to have a positive effect on the lungs [25].

The overall process is summarized in Appendix 1 (Anaesthesia decision tree).

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Authors

Version 3.0 (December 2020)

Working Group (in alphabetical order)

- Dr Christian Brunner MD
- Dr Olivier Huot MD
- PD Andreas Vogt MD

Expert Group (in alphabetical order)

- Dr Raphaël Giraud MD
- PD Franz Immer MD
- Dr Nathalie Krügel MD
- Dr Mathias Nebiker MD

Version 2.0 (August 2011)

Expert Group (in alphabetical order)

- Dr Peter Christen MD
- Prof Balthasar Eberle MD
- Dr Andreas Lüthi MD
- Prof Hans Peter Marti MD
- Dr Bruno Regli MD
- Dr Heinz Rieder MD
- Prof Frank Stüber MD

Version 1.0 (August 2009)

Working Group (in alphabetical order)

- Nicole Baehler
- Dr Catherine Blanc MD
- Dr Nicolas Dufresne MD
- Dr Yannick Mercier MD
- Dr Eduardo Schiffer MD
- Dr Jean-Luc Waeber MD

Expert Group (in alphabetical order)

- Prof Sylvie Bachy MD
- Dr François Clergue MD
- Frédéric Guibert
- Prof Christian Kern MD
- François Marguet
- Dr Maurice Matter MD
- Diane Moretti
- Bernard Mugnier

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Changes

Date	Version	Changes
February 2023	3.1	Corrections
December 2020	3.0	Revision, layout
May 2014	2.1	Layout and title adapted
August 2011	2.0	Update text
August 2009	1.0	Original Version



- Defibrillator in the vicinity
- Infusion solutions: preferably crystalloids
- Blood cells (leukocytes removed and CMV negative if recipient negative (++),
- Fresh frozen plasma, albumin and platelet concentrates if necessary, possibly PPSB
- Morphinomimetics (morphine, fentanyl sufentanyl (+)) Volatile anesthetic (sevorane)(+++) Vasoactive amines (noreprinephrine, adrenaline, isoprenaline, dobutamine) Ineffective atropine in brain-dead patients (++) Hypotensive agents (nitrated derivatives, sodium nitroprusside, αl-blocker) Short-lived beta-blockers (esmolol) Lidocarine Electrolyte solutions (calcium, magnesium, potassium) Heparin (3001U/kg) Complementary drugs (++) Diuretics (furosemide) Antibiotics by pathology and type of organs removed Corticosteroids: hydrocortisone (methylprednisolone if sampled from lungs) Desmopressin (Minirin®)/Arginine-vasopressin Other drugs as needed

Swisstransplant

Effingerstrasse 1 3008 Bern T: +41 58 123 80 00

info@swisstransplant.org www.swisstransplant.org

