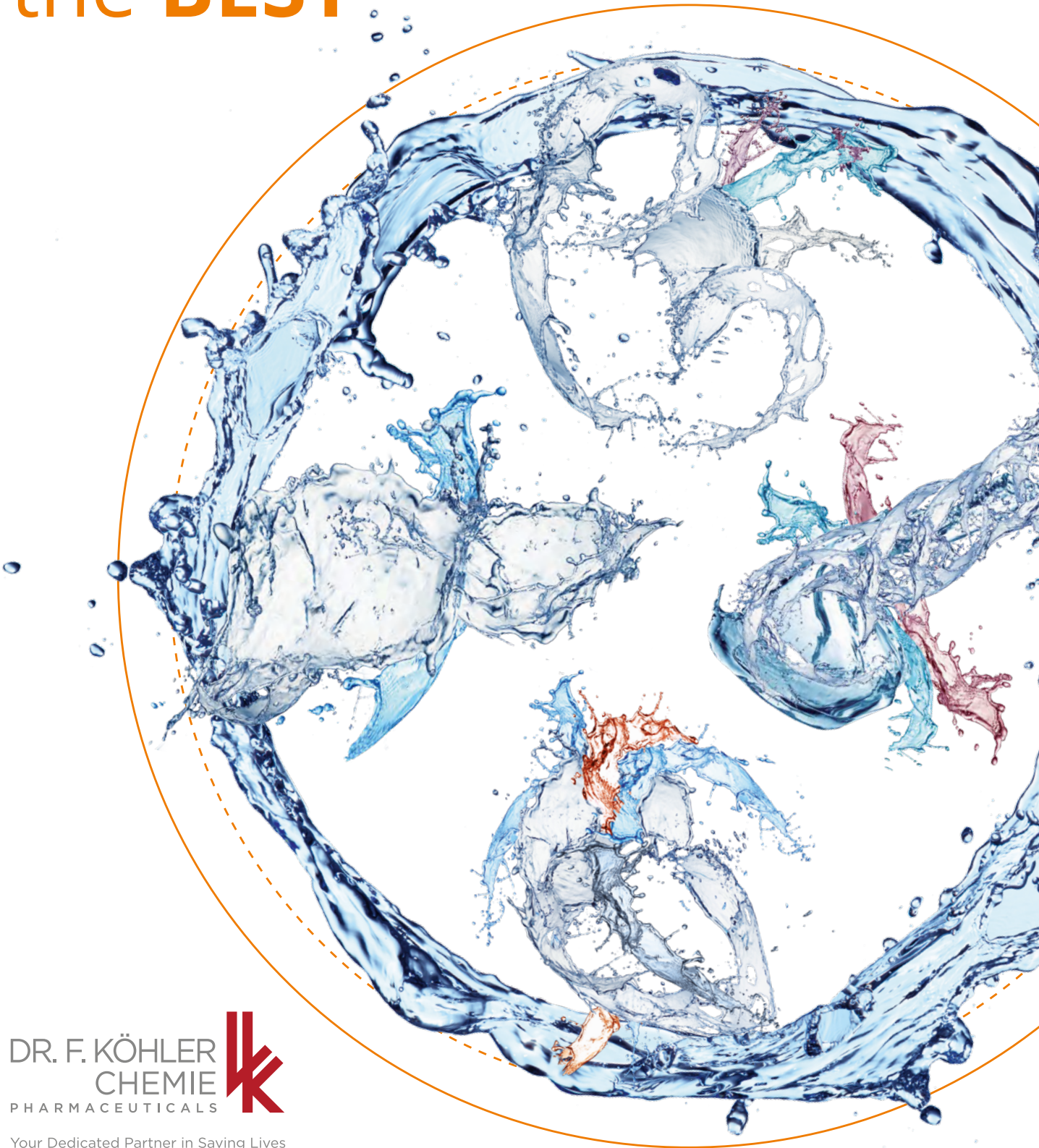


CUSTODIOL®

HTK - Bretschneider®

Every **ORGAN** deserves
the **BEST**

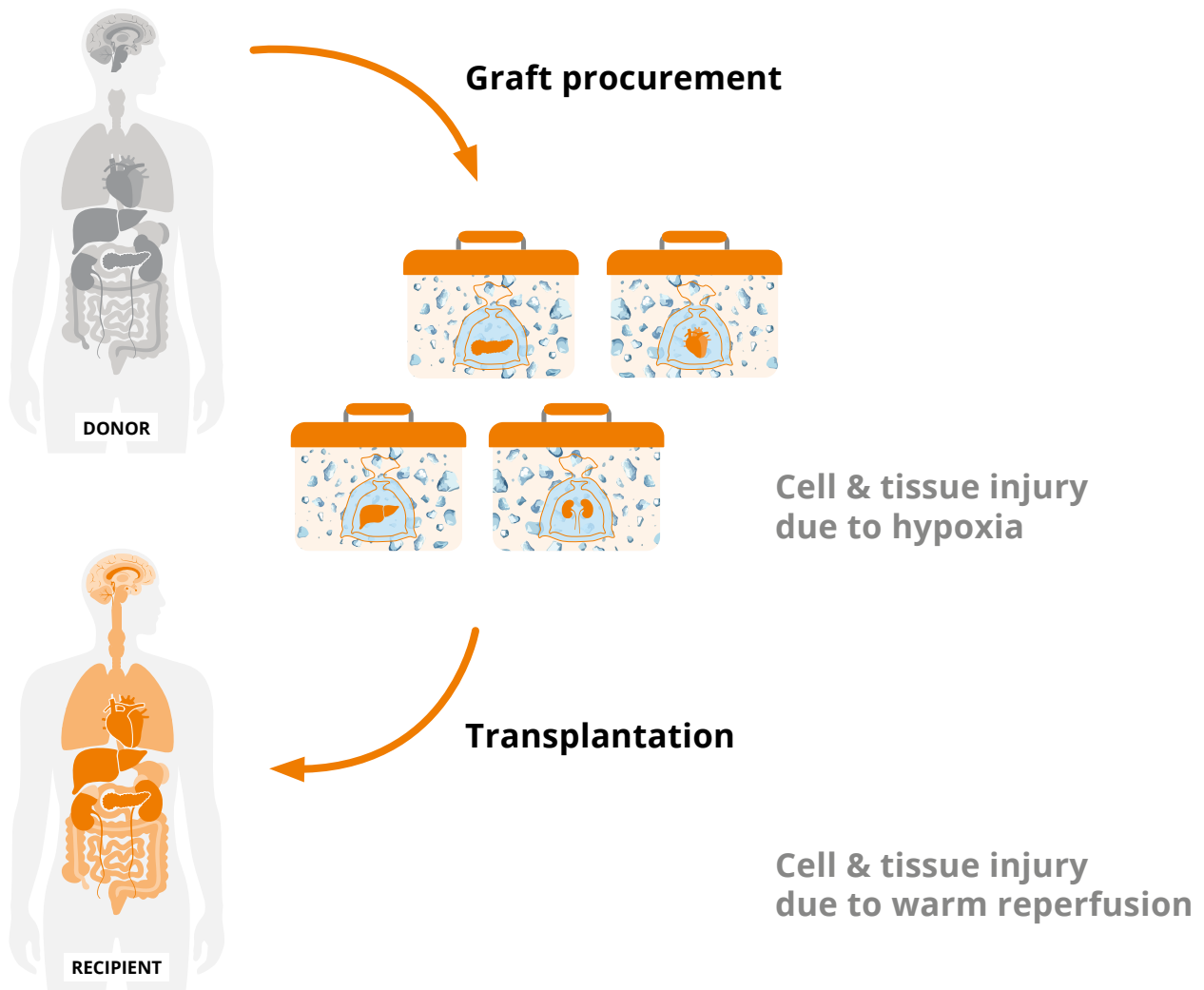


DR. F. KÖHLER
CHEMIE
PHARMACEUTICALS



Your Dedicated Partner in Saving Lives

THE PROBLEM: Ischemia Time during Transplantation¹⁻⁴



Max. natural ischemic tolerance of the abdominal grafts (liver, kidney, pancreas): 20–60 minutes^{5,6} and for the heart: 15–20 minutes⁷

Need for advanced ischemic protection strategies in organ procurement.

THE REQUIREMENT: Effective Preservation Solution^{2,4,8-10}

- Intracellular or extracellular electrolyte composition
- Strong buffering capacity to prevent acidosis
- Impermeant to prevent edema formation
- Scavengers of reactive oxygen species (antioxidants) to alleviate cellular stress and damage resulting from free radical formation
- Energy precursors which lead to higher levels of adenosine 5'-triphosphate (ATP) generation after ischemia and improved mitochondrial function
- Thorough washout of blood ("exsanguination") and catabolic products
- User-friendly handling (ready to use)

THE SOLUTION: CUSTODIOL®

CUSTODIOL® is an organ protection solution for the preservation of organ transplants (heart, kidney, liver, pancreas), together with venous or arterial segments, and multiorgan protection.¹¹⁻¹³

Histidine (180 mmol)^{10, 13-16}

- Strong organic buffer
- Prevents cellular acidosis
- Scavenger of reactive oxygen species (ROS)

Tryptophan (2 mmol)¹⁵⁻¹⁸

- Stabilizes the cell membranes
- Acts as an antioxidant that protects the organs against ROS-mediated damage

α -Ketoglutarate (1 mmol)^{15, 16, 19}

- Essential part of the Krebs cycle
- Energy substrate with a particular significance for the post-ischemic phase

Mannitol (30 mmol)^{10, 15, 16}

- Impermeant, prevents the formation of cell edema
- Scavenger of reactive oxygen species (ROS)

"Intracellular solution"^{8, 10, 16, 20, 21}

Low sodium (15 mmol) and calcium (0.015 mmol), moderate potassium (9 mmol) and magnesium (4 mmol)

- Cell membrane hyperpolarization and preventing conduction of an action potential
- Significant reduction of oxygen consumption of the organ

Histidine
Tryptophan
 α -Ketoglutarate

Mannitol

Sodium
Calcium
Potassium
Magnesium

The solution's water-like viscosity ensures optimal perfusion of the microvasculature.²² The isotonic **osmolarity** mitigates cell swelling and edema formation.^{15, 23}

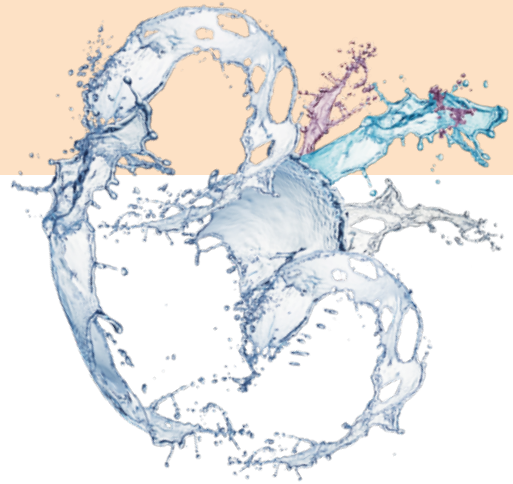
Due to its physiological composition (low potassium concentration), there is no need to flush out the solution prior to implantation.^{2, 24}

➤ The powerful combination of energy preservation, buffering against acidosis, and complete perfusion allows for safe and effective protection of organs during retrieval, transport and transplantation.



CUSTODIOL®

HTK - Bretschneider®



Indications

Preservation of organ transplants: perfusion and cold storage (kidney, liver, pancreas and heart)¹²

- Multiorgan retrieval & preservation
- Living donor transplantation (liver & kidney)
- For all donors (DBD, DCD and ECD)^{33,39}

Safe and effective preservation during retrieval, transport, and transplantation.



Powerful Organ Preservation^{4,25}

- The organic buffering system helps maintain physiological pH and reduces risk of acidosis.^{13,15}
- Mannitol and histidine contribute to antioxidant protection.^{14,16}
- Prevents hypercalcemia and intracellular edema formation.^{20,22}
- Ketoglutarate and magnesium ensure energy provision.^{16,54}



Practical and Economical Benefits

- Rapid washout of erythrocytes due to absence of colloids.⁵⁵
- Its water-like viscosity facilitates distribution in the circulation and enables faster cooling of organs.⁵⁶
- No additional washout required due to its physiological composition.^{2,24}
- Easy and safe to use⁵⁷: no additives required.
- Financial advantage associated with the use of CUSTODIOL® for liver^{24,58}, kidney^{59,60}, and pancreas transplantation.^{27,61,62}

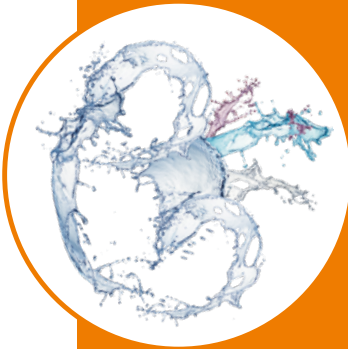


Decades of Trust

- Used in more than 3 million procedures worldwide.
- Referenced in over 1,000 publications.
- Approved for organ perfusion and preservation in many countries worldwide.



Powerful Organ Preservation^{4,25}



KIDNEY

- Proven safety and efficacy.^{26,27}
- Recommended as a renal preservation solution by the EAU guidelines 2023 (European Association of Urology).²⁸
- Considered a standard renal preservation solution in the Eurotransplant region.²⁹
- Low incidence of delayed graft function in living kidney donation.³⁰
- Lower rates of postoperative acute kidney injury (AKI) and hemodialysis compared to other perfusion types.³¹



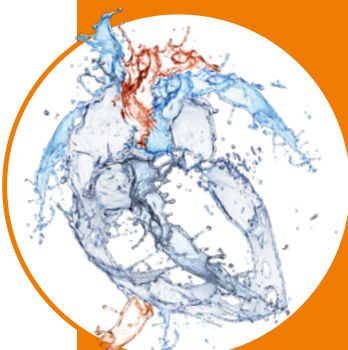
LIVER

- Preferred solution in the Eurotransplant region.^{32,33}
- Proven safety and efficacy.³⁴⁻³⁶
- Optimal graft survival even at long term follow-up.³²
- Recommended preservation solution for the protection against biliary complications.^{25,37,38}
- Superior preservation of DCD livers, including liver transplantation with cold ischemia times (CIT) of > 8 hours.³⁹
- Low viscosity and absence of HES improve microcirculatory perfusion.⁴⁰
- Recommended by the North American "best practice" guidelines for the preservation of the pediatric liver.⁴¹



PANCREAS

- Proven safety and efficacy for in situ perfusion and preservation.⁴²
- Excellent long-term survival at 10 years.^{43,44}
- Recommended by the First World Consensus Conference on Pancreas Transplantation 2019.⁴⁵
- Excellent outcomes in pancreatic islet isolation.^{46,47}
- Normal endocrine function during the first 6 months post transplantation.⁴⁸
- Low rates of pancreatitis (8%)⁴⁹ and of early thrombotic graft loss.⁴²



HEART

- Proven safety and efficacy.⁵⁰⁻⁵²
- Protection of hearts for 4 hours and more.⁵³
- Standard preservation solution for pediatric cardiac transplantation.^{54,55}
- Improved outcomes, including postoperative inotropic score, rejection score, 30-day mortality and midterm survival.⁵⁶

CUSTODIOL®

HTK - Bretschneider®

Composition: 1,000 ml of the solution contain: 0.8766 g sodium chloride (15.0 mmol), 0.6710 g potassium chloride (9.0 mmol), 0.8132 g magnesium chloride x 6 H₂O (4.0 mmol), 27.9289 g histidine (180.0 mmol), 3.7733 g histidine hydrochloride monohydrate (18.0 mmol), 0.4085 g tryptophan (2.0 mmol), 5.4651 g mannitol (30.0 mmol), 0.0022 g calcium chloride x 2 H₂O (0.015 mmol), 0.1461 g α-ketoglutaric acid (1.0 mmol), potassium hydroxide solution, water for injection. **Indications:** Cardioplegia in cardiac surgery operations, organ protection during operations under ischemia (heart, kidney, liver), preservation of organ transplants (heart, kidney, liver, pancreas). **Contraindications:** Hypersensitivity to the active substances or to any of the excipients. **Side effects:** During storage the two components histidine and ketoglutaric acid can convert to micropigment, which could block the angiotensin II receptors and thus might lead to a drop in blood pressure. **Warning:** CUSTODIOL® is not intended for systemic intravenous or intra-arterial administration, but only for selective perfusion of the relevant organs and for surface cooling and preservation of the donor organ en route from donor to recipient. CUSTODIOL® must therefore not be used for systemic infusion. **Presentation and pack sizes:** Bags of 1,000 ml, 2,000 ml and 5,000 ml. Prescription Drug. **Manufacturer:** Dr. Franz Köhler Chemie GmbH, Werner-von-Siemens-Str. 14-28, 64625 Bensheim, Germany. Sept 2024

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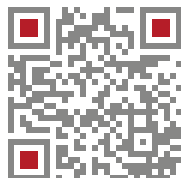
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