

HemoComp

outline for a new spin off company of the
Leibniz Institute of Polymer Research Dresden
& Max Bergmann Center of Biomaterials
(German Center of Excellence in Biomaterials)



Focus on Blood Contacting Materials

Extracorporeal devices

- Hemodialysis membranes
- Oxygenator membranes
- Hemoperfusion columns
- Tubings, disposables

Implants

- Vascular stents, stent grafts
- Vascular prostheses, shunts
- Heart valves, artificial hearts and cardiac assist devices

Common problems

Activation of hemostatic pathways

Inflammatory reactions

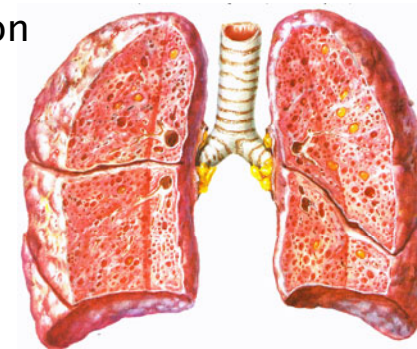
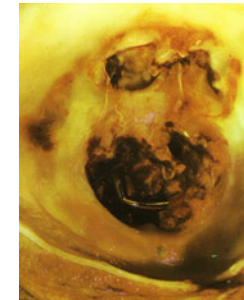
Hemolysis

Need for a more rational design and qualified evaluation of blood contacting surfaces

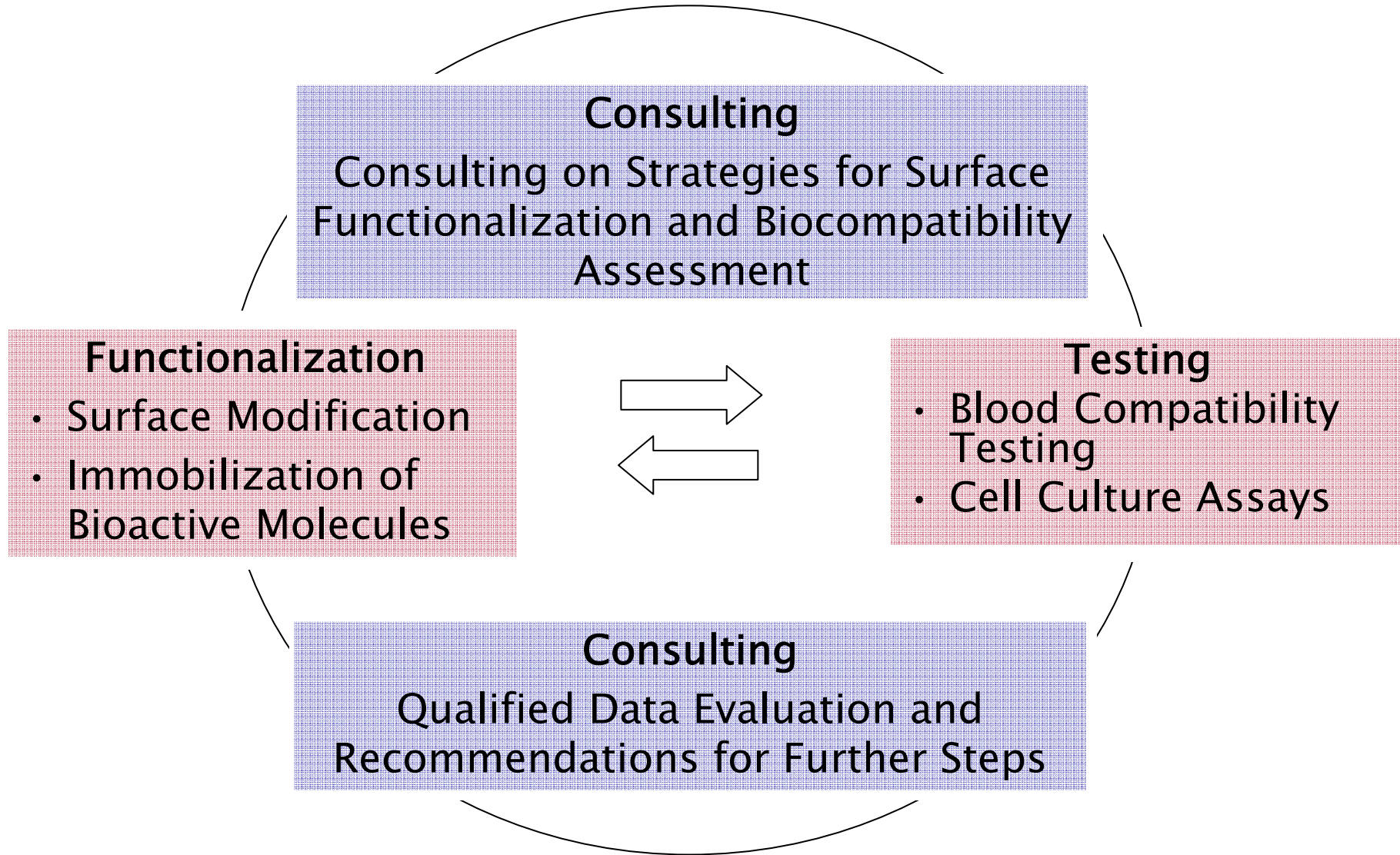


Undesired Side Effects of Medical Devices

- **Activation of blood coagulation**
 - Thrombosis → Embolia, infarction
- **Activation of blood platelets**
 - Thrombosis → Embolia, infarction
 - Leukocyte activation → Inflammation
 - Release of growth factors → Intima proliferation
- **Complement activation** → Inflammation, cell death
- **Activation of leukocytes**
 - Reactive oxygen species → Cell damage
 - Destructive enzymes → Matrix degradation, lung fibrosis
 - Cytokines and growth factors → Intima proliferation
- **Hemolysis**
 - Loss of red blood cells
 - Kidney damage by free hemoglobin
 - Platelet activation
- **Intima proliferation**
 - Restenosis → Repeated treatment necessary, infarction



The HemoComp Portfolio



The HemoComp Approach

HemoComp will provide the competitive edge for the rational design of hemocompatible coatings. This includes service for dedicated surface modification and testing of blood contacting biomaterials. Beyond that, HemoComp offers scientifically based consulting on strategies for surface modification and analysis.

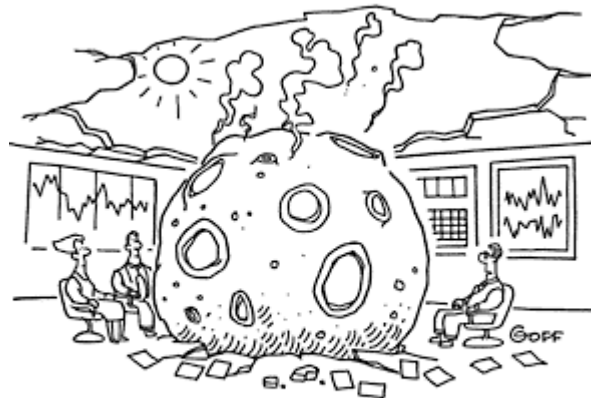
HemoComp is a spin off enterprise originating from the German Center of Excellence on Blood Contacting Biomaterials (Max Bergmann Center of Biomaterials Dresden) at the Leibniz Institute of Polymer Research. Certified hemocompatibility assessment can be provided in collaboration with ExCorLab GmbH.



HemoComp-Products I: Consulting

The Team

- is capable to share broad experience and knowledge in many aspects of **blood contacting surfaces**
- offers consulting on **customer-defined strategies** for surface functionalization and on their analytical evaluation.
- delivers a **scientifically sound interpretation** of experimental data and a thorough discussion based on the current literature.



"Is there anything else we failed to anticipate in our plan?"



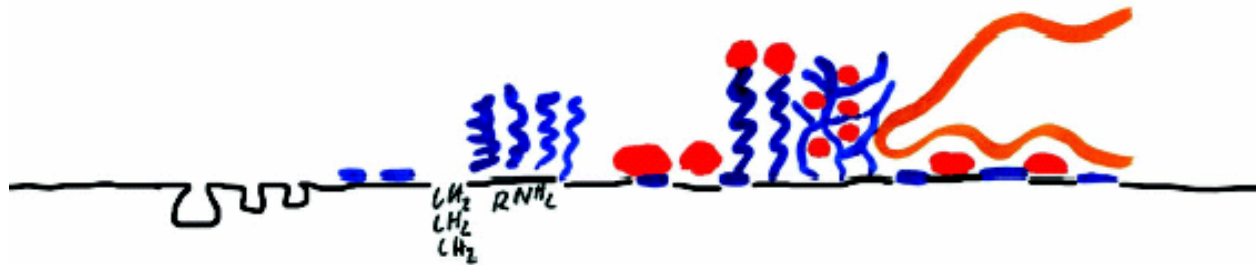
HemoComp-Products II: Functionalization Background and Principles

The performance of bioactive coatings is often limited

- due to inefficient orientation/linkage, degradation or structural changes of the bioactive elements and/or
- unspecific (secondary) adsorption of biopolymers

Options to address this problem include

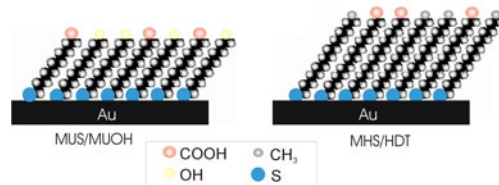
- the choice of the bioactive molecules (biopolymers, biomimetic molecules)
- the type of immobilization (anchorage, distribution, assembly of supra-molecular structures)



...need for molecular surface engineering platforms

HemoComp-Products II: Functionalization Physicochemical Surface Modification

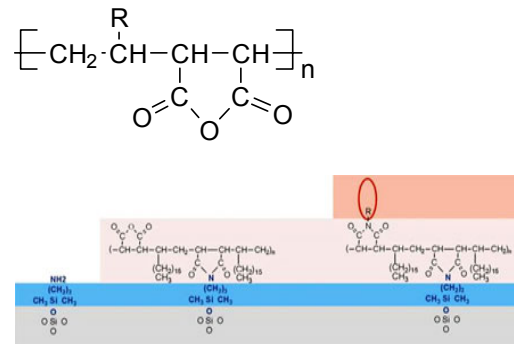
Self assembly of amphiphilic molecules



Schweiss, R., Welzel, P. B., Knoll, W., Werner, C.: Assembly Modulates Dissociation: Electrokinetic Experiments Reveal Peculiarities of the Charge Formation at Monolayer Films. **Chemical Communications**, 2005, **256**, 256–258

Schweiss, R., Pleul, D., Simon, F., Janke, A., Welzel, P. B., Voit, B., Knoll, W., Werner, C.: Electrokinetic potentials of binary self-assembled monolayers on gold: Acid–base reactions and double layer structure. **Journal of Physical Chemistry B**, 2004,

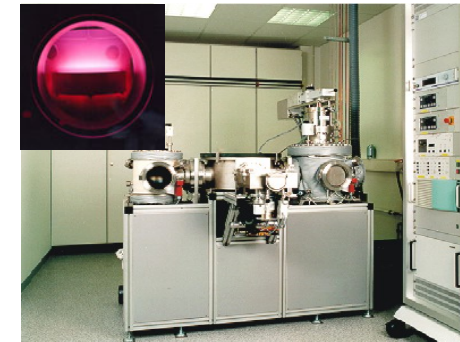
Reactive polymer coatings and their chemical conversion



Freudenberg, U., Zschoche, S., Simon, F., Janke, A., Schmidt, K., Behrens, S.H., Auweter, H., Werner, C.: Covalent Immobilization of Cellulose Layers onto Maleic Anhydride Copolymer Thin Films. **Biomacromolecules**, 2005, **6**, 1628–1634

Pompe, T., Renner, L., Grimmer, M., Herold, N., Werner, C.: Functional Films of Maleic Anhydride Copolymers under Physiological Conditions. **Macromolecular Bioscience**, 2005, **5**, 890–895

Low pressure plasma and electron-beam treatment



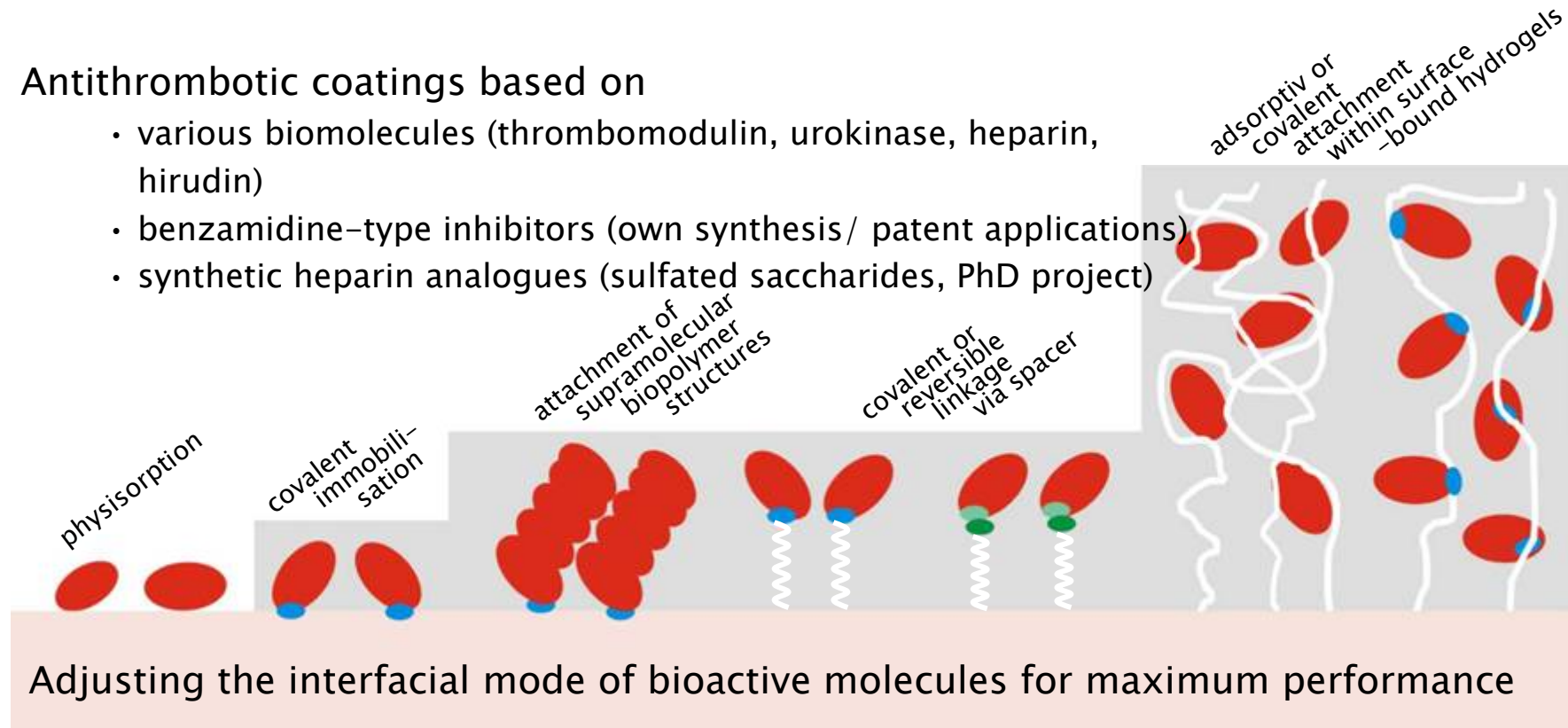
Meinhold, D., Schweiss, R., Zschoche, S., Janke, A., Baier, A., Simon, F., Dorschner, H., Werner, C.: Hydrogel characteristics of electron-beam-immobilized poly(vinylpyrrolidone) films on poly(ethylene terephthalate) supports. **Langmuir**, 2004, **20**, 396–401

Nitschke, M., Zschoche, S., Baier, A., Simon, F., Werner, C.: Low Pressure Plasma Immobilization of Thin Hydrogel Films on Polymer Surfaces. **Surface & Coatings Technology**, 2004, **185**, 120–125

HemoComp-Products II: Functionalization Immobilization of Bioactive Molecules

Antithrombotic coatings based on

- various biomolecules (thrombomodulin, urokinase, heparin, hirudin)
- benzamidine-type inhibitors (own synthesis/ patent applications)
- synthetic heparin analogues (sulfated saccharides, PhD project)



- Salchert, K., Gouzy, M., Glorius, M., Kühn, A., Nitschke, M., Werner, C.: Immobilization of an Anticoagulant Benzamidine Derivative: Effect of Spacer Arms and Carrier Hydrophobicity on Thrombin Binding. *Acta Biomaterialia*, 2005, 1, 441-449
- Sperling, C., Salchert, K., Streller, U., Werner, C.: Covalently immobilized thrombomodulin inhibits coagulation and complement activation of artificial surfaces in vitro. *Biomaterials*, 2004, 25, 5101-5113
- Gouzy, M. F., Sperling, C., Salchert, K., Pompe, T., Uhlmann, P., Streller, U., Rauwolf, C., Simon, F., Böhme, F., Voit, B., Werner, C.: In vitro Blood Compatibility of Polymeric Biomaterials through Covalent Immobilization of an Amidine Derivative. *Biomaterials*, 2004, 25, 3493-3501
- Pham M.T., Reuther H., Maitz M.F., Native extracellular matrix coating on Ti surfaces. *Journal of Biomedical Materials Research* 2003; 66A: 310-316.
- Patent Application DE 10329296: Beschichtungssystem für Biomaterialien.



HemoComp-Products III: *In vitro* Blood Compatibility Testing

Test parameters:

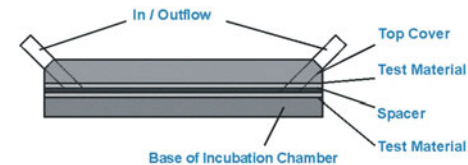
- Cell count before and after the incubation
- Blood gases
- Thrombin-Antithrombin complex (TAT)
- C3a, C5a, sC5b-9
- Platelet Factor 4
- Scoring of number and shape of adherent platelets



Incubation systems:

A static screening chamber and a dynamic 'perfusion set-up' have been developed and evaluated for the for the blood compatibility tests. Advantages over other methods:

- No blood-air contact
- Adequate area ratio of sample/container surface
- Inert container material
- Constant temperature
- No sedimentation



- Sperling C, Houska M, Brynda E, Streller U, Werner C. In vitro hemocompatibility of albumin-heparin multilayer coatings on polyethersulfone prepared by the layer-by-layer technique. **Journal of Biomedical Materials Research Part A**. in print 2006
- Maitz M.F., Shevchenko N. Plasma immersion ion implanted nitinol surface with depressed nickel concentration for implants in blood. **Journal of Biomedical Materials Research Part A**. 2005; 76A: 356-365.
- Maitz M.F., Gago R., Abendroth B., Camero M., Caretti I., *et al.*, Hemocompatibility of low-friction boron-carbon-nitrogen containing coatings. **Journal of Biomedical Materials Research Part B: Applied Biomaterials**. in print 2006
- Sperling C, Schweiss RB, Streller U, Werner C. In vitro hemocompatibility of self-assembled monolayers displaying various functional groups. **Biomaterials** 2005; 26(33):6547-6557
- Streller U, Sperling C, Hubner J, Hanke R, Werner C. Design and evaluation of novel blood incubation systems for in vitro hemocompatibility assessment of planar solid surfaces. **Journal of Biomedical Materials Research** 2003; 66B(1):379-390

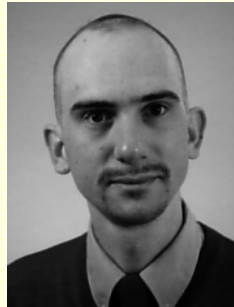


The HemoComp Team



Claudia Sperling

- Biologist, PhD
- Laboratory head and group leader at IPF/MBC
- 8 years of experience in the *in vitro* hemocompatibility assessment of biomaterials



Manfred Maitz

- Physician, MD
- Scientific coworker at IPF/MBC
- Over 10 years of experience in the biological evaluation of biomaterials



Marie Françoise Gouzy

- Chemist, PhD
- Laboratory head and group leader at IPF/MBC
- 5 years of experience in synthesis and immobilization of coagulation inhibitors



Carsten Werner

- Chemist, PhD
- Head of the IPF-groups at MBC
- Adjunct Professor at the University of Toronto, Canada
- Background in Surface Chemistry/Biophysics

The Host Institution of HemoComp

The Max Bergmann Center of Biomaterials Dresden is a joint interdisciplinary initiative of the Dresden University of Technology and the Leibniz Institute of Polymer Research Dresden. A state-of-the-art laboratory building covers workspace for about 100 coworkers including

- Chemical laboratories
- Polymer processing equipments (e. g. GMP melt spinning plant)
- Laboratory for bioanotechnology
- Laboratories for surface modification (e. g. plasma treatment) and characterization (physico-chemical, biochemical and cell-biological methods of analysis)
- Biocompatibility testing techniques (whole blood incubation, cell culture)
- GMP class A facilities for sterile preparations



MAX BERGMANN
center of biomaterials dresden

Partnership for Enhanced Performance and Service

EXcor**L**ab GmbH

Close collaboration with the certified testing laboratories of the ExcorLab GmbH (<http://www.excorlab.de>, Managing Director Dr. Horst-Dieter Lemke)

- certified in vitro hemocompatibility testing
- animal models and clinical studies (in particular to evaluate extracorporeal artificial organs)
- outstanding expertise in product certification

The founders of HemoComp closely collaborate with Dr. Lemke for more than one decade on membranes for blood purification and on the hemo-compatibility assessment of various biomaterials.



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