# plastic solutions

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MEDICAL PLASTICS
PROCESSING DIVISION

# CONTENTS




# Medical Engineering – a Key Technology

**GEMÜ GmbH Switzerland: System Solutions in Plastics for Medical Engineering**

## Dear Reader,

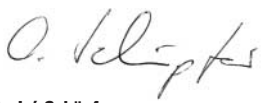
Our strategic decision to provide system solutions in plastics also for the medical engineering field has proved to be a very clear confirmation of our technological policy. In the meantime we are already producing highly sterile plastic components for autologous chondrocyte implants and shall shortly be starting serial production in other very demanding medical projects. Based on the background of our own experience we can therefore justly make the claim:

**Among the key technologies, medical engineering is at the very forefront!**

We are not alone in this opinion. Medical engineering companies that are quoted on the stock exchange have also come to the same conclusion. Even companies that are not involved in this field make the same prognosis. This is shown, for example, by the "Key Technologies in 2010" study carried out by the Electrotechnology, Electronics and Information Technology Association (VDE). In this study the importance of the individual key technologies is assessed differently. According to the opinions of the 300 specialists from the universities and industry who were questioned, biotechnology and medical engineering, especially in the fields of diagnostics, surgery and implantation technology, stand in first place.

In this issue you will find a lot that is new in the field of medical engineering. For example you will learn how we are involved and how we have been able to become established in this interesting market in a very short time. Or how we are able to convince and please medical doctors and biologists with clean-room technology and customer-oriented project management. We are constantly striving to maintain this high standard that we have set ourselves. You will also find a lot of interesting information on the present status of medical engineering.

I wish you enjoyable reading.



**André Schüpfer**
**Managing Director, GEMÜ GmbH Switzerland**

# Utilise Synergies and Build Up Strengths

André Schüpfer, Managing Director, GEMÜ GmbH Switzerland

**GEMÜ Switzerland has been working successfully for many years in the fields of valve, measurement and regulating systems. Since a couple of years the company, which has its Headquarters in Rotkreuz, Zug, is making a name for itself in the field of medical device engineering. The Managing Director, André Schüpfer, was interviewed for GIT VERLAG.**

*Interviewer: Christoph Hug*

**GIT VERLAG: Mr. Schüpfer, for the past 22 years you have been Managing Director of GEMÜ GmbH Switzerland. In which core competences is GEMÜ Switzerland particularly strong?**

**André Schüpfer:** Our main strength clearly lies in the plastics field. Here at Rotkreuz we are in the process of building up the centre of competence for the whole GEMÜ Group. The whole injection-molding operation is also concentrated in Switzerland. Also at Rotkreuz, we are at present further building up our competences in the new business sector, "Medical Engineering". An innovative Research and Development Department has already been set up in this field. I am especially proud of this department.

**The medical sector is not a simple field of activity. What led you to enter this business sector?**

**André Schüpfer:** We have been manufacturing products under clean-room conditions with great success for the past ten years. And we already have a great wealth of experience in this field. Up till now we have been using our clean-room production facilities mainly for customers in the biology-related fields and in the semi-conductor industry. We make use of our know-how and extend into the field of medical engineering.

**Experience in production is the one side. The other side is personal know-how in research and development, as well as in project management. What measures have you taken to ensure success in this new field of activity?**

André Schüpfer: We have a centre of competence for the medical engineering sector. With Lars Rominger and Philipp Bächtold we have two outstandingly well-trained specialists. We are also working very closely with Dr. Frank Stieneker of the Working Association for Pharmaceutical Process Engineering (AVP). The AVP is a scientific public-welfare association with its headquarters and offices in Mainz, Germany. Frank Stieneker is a proven expert in the field of medical engineering.
There is also a new collaboration with the Institute for Applied Process Optimisation (IFAP). Together with Peter Thaler of the IFAP we shall be constantly optimising all the different processes. Although here the economic efficiency of the processes is the prime consideration, thanks to the process optimisation it is also possible to guarantee the purity of the products. And thanks to certain process innovations we have one of the best clean-room production facilities available.

**You first entered the medical field in 2003. How satisfied are you with what you have achieved up till now?**

**André Schüpfer:** We in fact expected to complete our first projects only towards the end of 2004. But now we have already successfully completed some projects. Which means that I am very satisfied with our entry into this field. And with these projects we have also been able to give our customers absolute satisfaction.

**What do you think are the reasons for your rapid and successful entry into this new field?**

**André Schüpfer:** On the one hand a little luck certainly plays a role. On the other hand we have


always been very uncomplicated in the way we work and determined in our approach to the different projects. Our customers appreciate this and they trust us. With the existing Intranet we also have an outstanding tool for project management. With this, we are able to keep in close contact with the customer at all times. Thanks to "https", all the persons involved have direct access to the present status of the project, round the clock.
So much for our success in the medical field. There is in fact in general a very good working atmosphere at GEMÜ. In all our activities we have always been very customer-oriented and we are also very flexible. This is also very much appreciated by our customers in the medical field. Looking at it in this way, we have achieved a foothold in the medical engineering field simply on the basis of our existing strengths.

**Your success in the medical field also depends on the availability of resources in Production. Is there perhaps a bottleneck here, or have you already planned an expansion of the production facilities?**

**André Schüpfer:** At the moment there is not a bottleneck in this respect. The centre of competence in the plastics field, like that in the medical field, is in a constant state of development. However, for these two new business sectors we shall soon need more space, which will in fact be made available to us by the end of 2005, at the latest. The first phase is already underway: the updating of the energy supply – water, electricity, air and air-conditioning – has already been completed. In the second phase a new middle section will be built, and in Phase 3 we shall incorporate all the external production facilities into this new middle section. At the beginning of 2006 we shall have brought together all the external production facilities on the one site. In recent years – because of our considerable growth – we have also had to rent external premises for parts of the production.

**Although your activities in the medical field have been built up quite fast, they are already very successful. How do you see the potential for improvement in the future?**

**André Schüpfer:** We are doing everything possible to develop the products even more in accordance with our customers' needs. Thanks to the joint product development we shall be in the position to bring the products onto the market even faster. In the present market situation this is very important.

**You have been working at GEMÜ for the past 22 years. In this time you will certainly have experienced ups and downs in the company's fortunes. What do you remember most?**

**André Schüpfer:** The "low" that I remember best is the downward trend in the semi-conductor industry, but we have in the meantime also overcome this problem very well indeed.

As a "high" I would particularly mention the overall success of GEMÜ on the market in general. We are now among the leaders, worldwide, especially in the biological and semi-conductor sectors. We achieved the same objectives in the field of medical engineering.

**Mr. Schüpfer, I would like to thank you very much for talking to us.**

**About our interviewee:**
André Schüpfer has been working at GEMÜ GmbH in Switzerland for the past 22 years and knows the company's history extremely well. Previously, this dynamic family man had worked with the firms ESEC and Schindler. At the start of his career with GEMÜ, besides his work in management he also was involved in practical work in the Production department. This is why even today he is regularly to be found on the Production floor. He just likes being there, and the regular contact with the employees is also very important to him. André Schüpfer is married and has two grown-up daughters.

# Innovations for Human Health

*Philipp Bächtold*

**Over the next few years fundamental changes are to be expected in the field of medical engineering: "Smaller, more pleasant and safer" is the motto. Also, thanks to new, innovative products and the surgical techniques for which they will be used, the costs in the health sector will be reduced.**

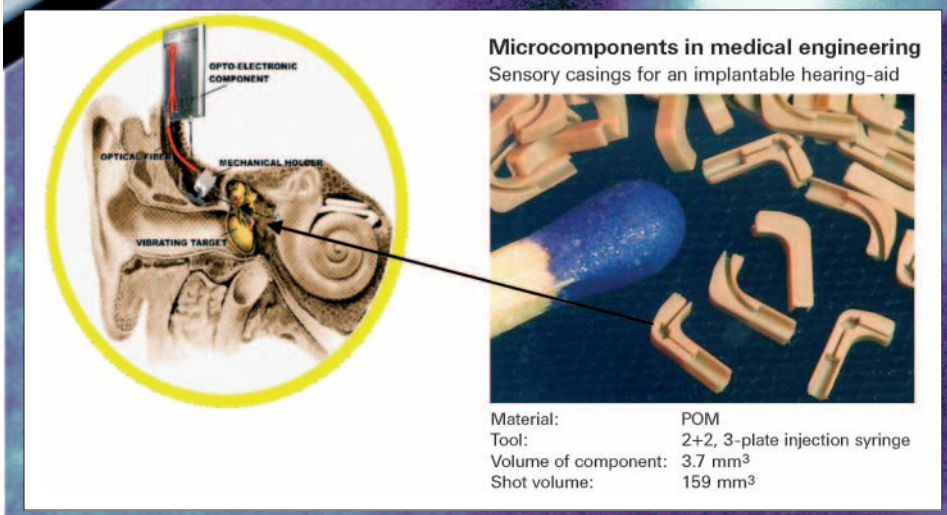
Developments in the health sector can be compared absolutely with those in the IT field. Instead of "smaller and faster", in the health sector the motto is "Smaller, more pleasant and safer". This development is not going to stop over the coming years. Modern medical engineering will bring decisive changes in our health sector. In the future the latest technology will make new surgical solutions possible. These technologies will in turn depend on the advances in the material technologies. Plastic components play an important role in these technological advances.

## (Replacement) Components for the Human Body

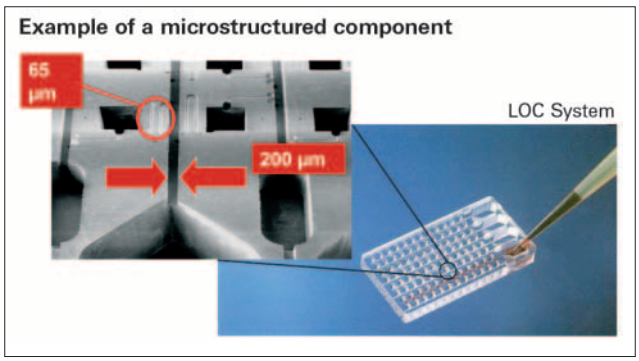
New plastic materials and their processing procedures help, in part, in the development and manufacture of medical components which represent an economical single-use replacement for sterilisable products. This results in two major advantages. Firstly, the single-use components reduce the potential for error in the cleaning and sterilisation by the hospital personnel. Secondly, with the use of these products hygiene is improved, thus increasing the safety for the patients. Also, these single-use components meet the ever-increasing demands of the health insurances for lowering of the costs.

## Miniaturisation on the March

Thanks to the innovations in plastics technology, in future smaller components with more variations will generally be possible. Here too, the trend towards miniaturisation is fortunately proceeding apace. These plastic components are at least equally as safe as conventional components. Thanks to new plastic materials and new procedu-




**Very small functioning components are today no longer a problem in plastics technology (right). The hammer, the anvil and the stirrup bone can today be "mass produced" from plastic components. Thanks to their implantation, hearing becomes possible again.**
(Illustration: Battenfeld Extrusionstechnologie GmbH, Germany)




**The health sector is going through the same changes as the computer world. Small and more exact solutions: Left: Close-up of the lab-on-a-chip. Right: Lab-on-a-chip for the blood analysis.** (Illustrations: STEAG microParts GmbH, Germany

res for the processing of plastics, extremely small (replacement) components for the human body can already be manufactured today. Also new ways of administering drugs are being opened up.

Besides miniaturisation, many innovations in the field of medical engineering reflect certain fundamental trends in the health sector: for example, the better tolerability of the materials and shorter treatment and convalescence times. Certain components or devices are in fact "made to measure" for the person to be treated. One example of this is the implantable hearing-aid (see illustration).Hammer, anvil and stirrup bone can today be produced from plastic granulate. Thanks to these artificial "micro-components", in the event of damage to one or more of these parts the hearing can be restored. Thanks to the miniaturisation of specific medical components, a doctor is generally able to use more targeted therapies. For example, thanks to the very much smaller cardiac pace-makers that are now available, these can today also be used in children, a thing that was practically impossible in the past. Today heart valves in very small sizes can also be made from plastic material. For example, a plastic heart valve adapted to the size of the patient can also be used in children. The heart valve "grows", so to speak, with the patient. In future the replacement of heart valves will be possible as a minimally invasive operation, without the need for open-heart surgery. The first trials are already proving to be very promising.

## Increasing the Quality of Life

The manufacture of (replacement) components for the human body represents only one aspect of the developments in the medical field. New ways of administering drugs are a second important field. As one example among many others, the administration of insulin without needles may be mentioned here. This method of administering insulin is made possible by intelligent plastic components. Small implanted insulin-pumps make constantly repeated injections with the needle unnecessary, and hopefully in the near future intelligent insulin-pumps will also be used. Then, these small plastic components will notice, automatically, what dose of the drug has to be administered, and when. This is today already the case with the intelligent cardiac pace-makers, which react to changes in the body with a higher or lower pace-maker frequency.

## Cost-saving Blood Analyses

Many researchers are working in a third field: the manufacture of medical devices. Here it is mainly a question of saving costs, but at the same time also of maintaining at least the same safety standards. In the case of innovations, however, these standards are as a rule exceeded.

One example of the current research and development is in the field of blood analyses, where two objectives are being pursued simultaneously. On the one hand, the aim is to increase the capacity of the analytical machine, while on the other the aim is to reduce the amount of blood that is needed for the analysis. In this way both costs and valuable time can be saved at the same time, and also the patient has to give less blood. It is planned that in future, with the same mechanical principle, no longer will only fifty analyses be carried out simultaneously, but around two thousand. The solution to this problem is obvious. The containers for the blood samples must at the same time be smaller and more exact (see illustration), which a few years ago would have been impossible but which today, although still not standard procedure, is possible.

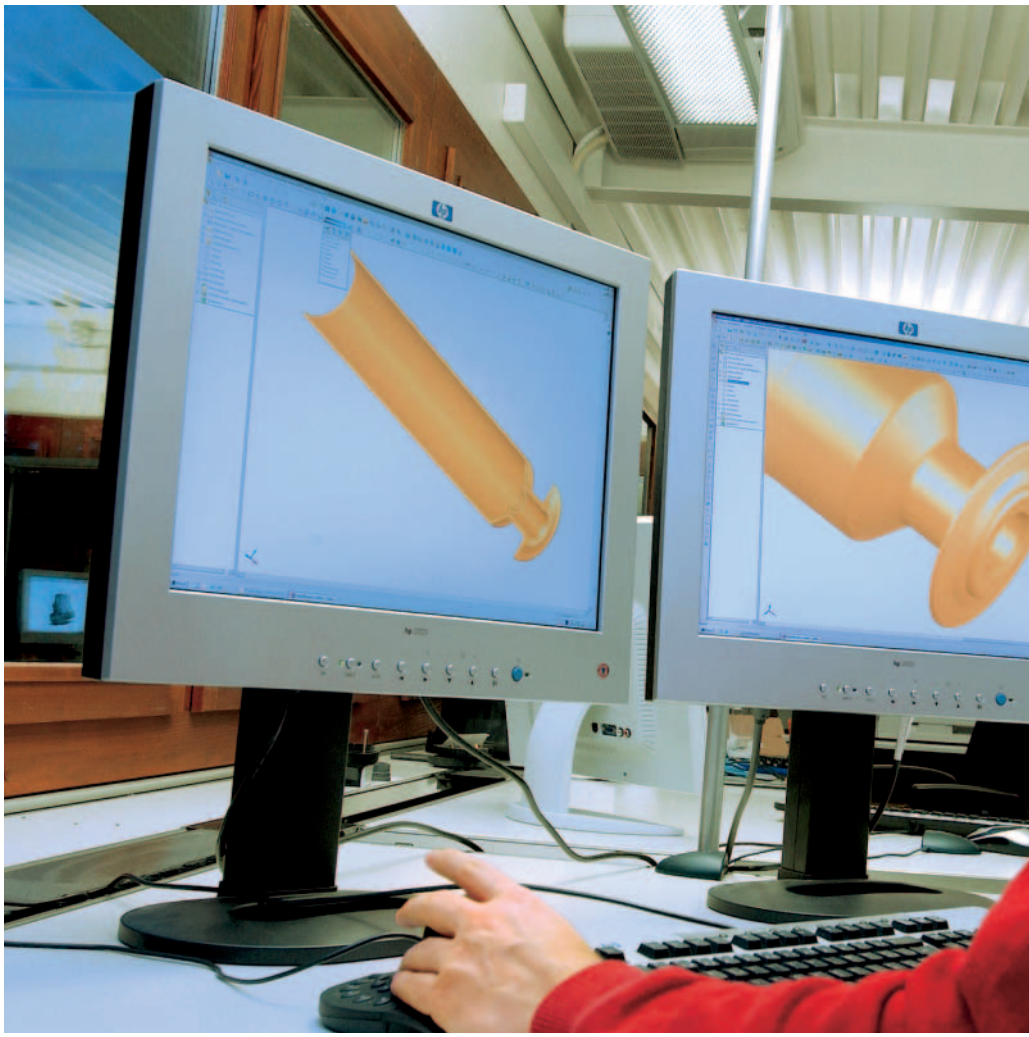
## Developments in the Medical Field: GEMÜ at the Forefront

With its own Research and Development Department, GEMÜ GmbH Switzerland is right at the forefront in the key technology – medical engineering. The firm combines its own experience in the development and manufacture of complex, high-quality plastic components with the professional competence of medical doctors and scientists. Together with its partners, GEMÜ develops target-oriented, practical and safe solutions, details of which are to be found in the following articles in this specialist journal.

**About the author:**
Philipp Bächtold is Head of Technology/Design/Development, Medical Engineering, at GEMÜ GmbH Switzerland.

# Cost Efficacy and Value of Time-tested Systems in Clinical Diagnostics

Lars Rominger



**Several times in the recent past, heads of central laboratories and those in charge of purchasing and procurement in clinics have been faced with the decision as to whether they should invest in new medical technologies. In most instances the criteria for decision-making are clear, demonstrable, and can be evidenced in terms of economic efficiency as well as the medical value of the technology. However, in some instances technological advances are the only driving force for those offering new products in this sector. For laboratory executives this means that a clear system-based margin must be drawn between new investments in uncertain products on the one hand, and the stable, safe and continued application of time-tested systems and processes on the other.**

**About the author:**
Lars Rominger is Head of Marketing/Sales, Medical Engineering, at GEMÜ GmbH Switzerland.

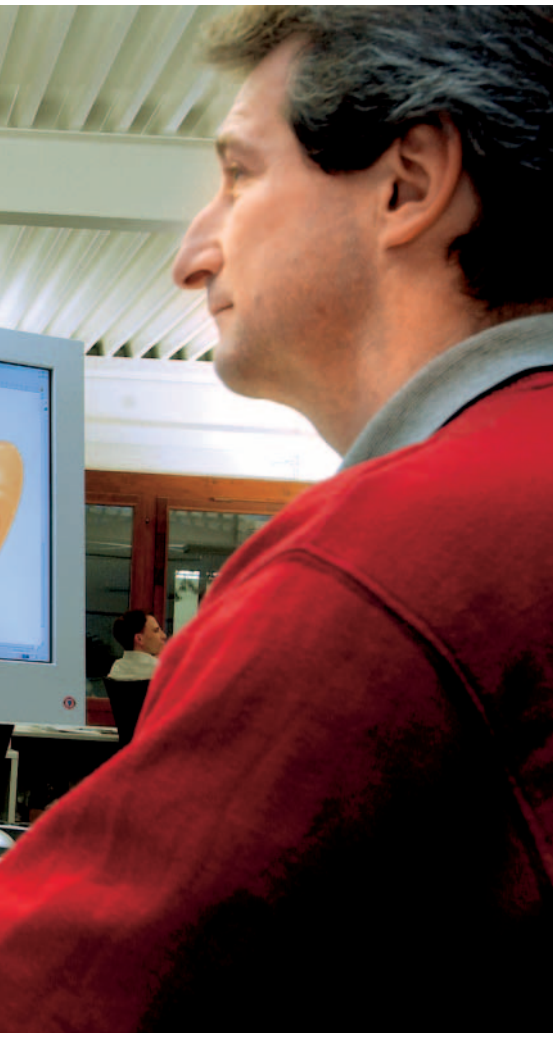
For several years now there has been a quest for a time-tested, safe, medically stable, financially established and economical principle in medical diagnostics. Human blood for analysis is centrifuged. By this process blood is fractionated into two phases: the blood clot remains below and the serum is collected above. After centrifugation a blood filter is introduced into the centrifuge glass and the serum is filtered. This standardized procedure is used to filter out any residual clots or other components that may still be present in the fluid above.

The purpose of this filtering procedure is to avoid any risk of falsifying the test result and also prevent sedimentation in the instruments used for analysis.

## Gel versus Blood Filter

This standardized procedure is being applied successfully for several years and is now established as a standard in nearly all laboratories. The system is time-tested and absolutely reliable. The use of blood filters produces reliable test substances for the subsequent measurement. The company that has been manufacturing this product so far recently informed its market partners that the above mentioned blood filter will no longer be produced or distributed. It was also stated that the manufacturing companies, after several years of intensive and laborious research, are now backing a procedure that will gradually replace the previous system and also simplify it. A principle based on a gel procedure was developed and the product manufactured according to this principle. Separation gel tubes are in use for a few years now. They were developed to improve the process of preanalysis. The production of the blood filters was stopped because the manufacturing company presumed that the increasing use of separation gel tubes would replace the blood filters. The manufacturer is actively working on marketing and introducing the new gel-based procedure. However, according to users in central laboratories, the market maturity of this procedure is highly disputed, although the technology of analysis instruments has made significant progress.

As the production and delivery of the manufacturer's time-tested and esteemed blood filters has been suspended, laboratory executives were now



being forced to focus their attention and interest exclusively on the gel-based procedure. In the current environment of cost-sensitivity and economic pressures in the public health sector, requests for investments in new devices and/or systems are received with little enthusiasm by the financial departments of medical clinics.

The situation is rendered more difficult by the fact that personnel – in this case medical laboratory staff – have to be re-trained within the hospital. In addition to new investments, this change involves additional effort in terms of training time and monetary resources for re-training materials.

In every case, decision-makers among the medical staff are mainly concerned with maintenance of the service unit, work processes, and the required purity and reliability of blood samples. One of the aspects of the core competence of a laboratory is its ability to deliver a large number of absolutely reliable blood analysis within a short period of time. This requirement must be fulfilled. It poses a challenge, particularly for medical technology.

Seventy staff members are employed by GEMÜ GmbH (private limited company) in Switzerland - a competence center for plastics and medical technology, part of the GEMÜ group which operates on a worldwide basis, with its head office in the town of Ingelfingen-Criesbach close to Stuttgart (Germany). The GEMÜ enterprise is active in the fields of medicine, medical technology, the pharmaceutical and food industry, process engineering and microchip production. Processing technology at GEMÜ GmbH in Switzerland focuses on the injection molding of plastics. In this sector the company offers system-based solutions for plastics in the medical industry, in biotechnology, the semiconductor and electronics industry. At the Swiss office in Rotkreuz, extensive resources have been invested over the last few years in clean room concepts for the production of medical-technical products. GEMÜ engages more than 850 staff members throughout the world.

## Re-launching of Time-tested Products

Based on a market analysis, the managers of GEMÜ GmbH in Switzerland recognized the precarious situation early and developed measures to resolve this critical state of affairs. Within a short period of time, a task force under Lars Rominger was established within the company and empowered with the authorities required to do the job. In a few weeks the task force designed an innovative system-based solution to the problem, based on stringent process-oriented project management. This was the driving force behind the newly developed serum filter **Seraclean** – a solution to fulfill a specific need, offered at a price in line with market conditions.

The product specifications provide evidence of GEMÜ GmbH's (Switzerland) extensive specialized know-how in the field of system-based solutions in plastics for medicine and the industry.

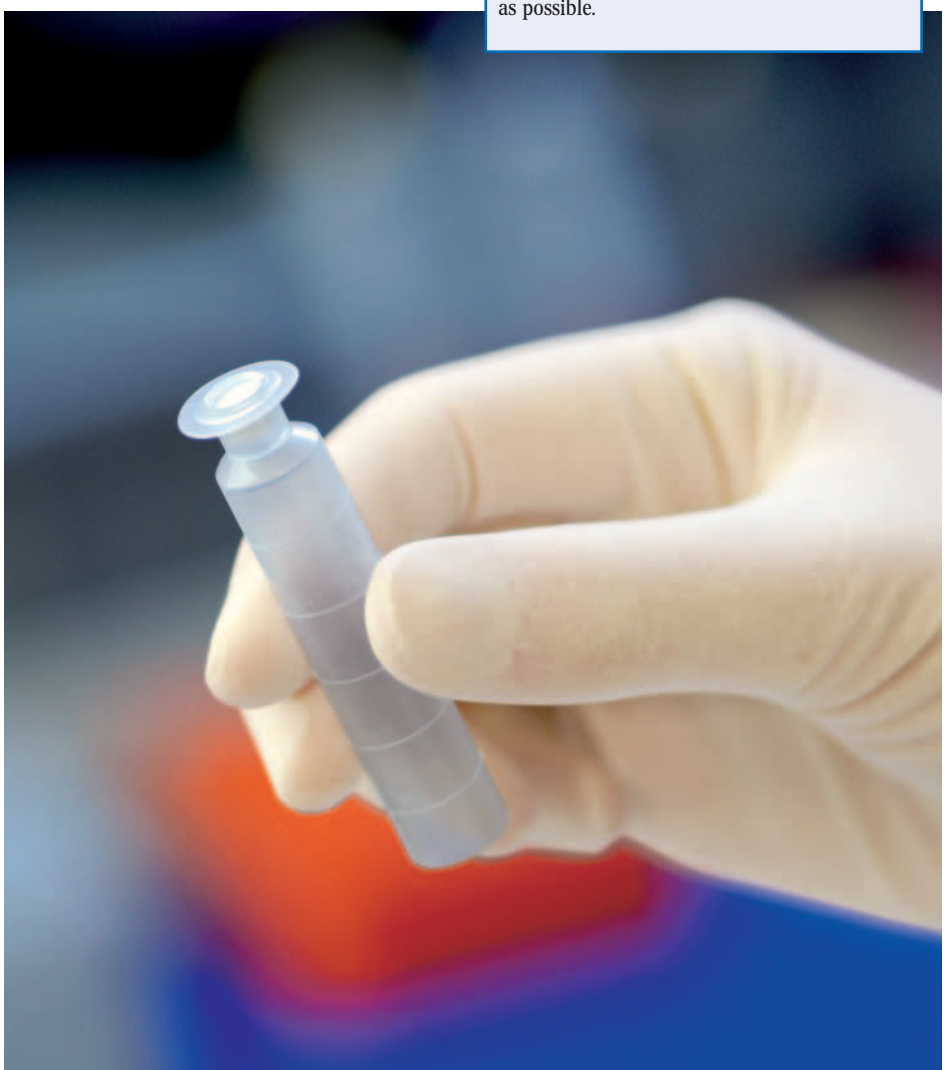
## The Products and how they Work

Human blood for analysis is centrifuged. By this procedure blood is fractionated into two phases: the blood clot remains below and the serum is collected above. After centrifugation, a blood filter is inserted into the centrifuge glass and the serum filtered by this procedure. The purpose of this standardized process is to filter out any residual clots or other components in the fluid above.

## Integrated Additional Technical Value

In contrast to other filter systems Seraclean is equipped with a sealing-lip that never ceases to function because of the specific tool manufacturing technology and the manufacturing processes used to produce this instrument.

Besides, based on a number of detailed technical discussions with laboratory executives and users of serum filters, Seraclean has been designed such that it provides maximum functionality while its application is as user-friendly as possible.



## Market Acceptance from the 0 Series Onward

In numerous conversations and detailed hearings with clinical laboratory executives, both the task force and the executives of GEMÜ received adequate confirmation of the necessity and appropriateness of this developmental project. A re-launch of a long-standing time-tested serum filter on a high-tech synthetic basis, in line with the highest standards of clean room technology, is a high-level market opportunity. Market partners at all levels of the hierarchy and in all positions have asked for a simple and safe product in alignment with real market conditions. The acceptance of the newly introduced **Seraclean** filter in the market is an undisputed fact. This was confirmed in several conversations that Lars Rominger held with Dr. Engler and Ms. Bossart from Kantonsspital St. Gallen (Institute for Clinical Chemistry and Hematology), and Lukas Bestmann, Head of the Department of General Analytics from the University Hospital of Zurich (Institute for Clinical Chemistry).

## The Direct Advantage for the Client is Self-evident:

- The instrument requires no new financial investments in central laboratories. It involves no costly revisions of specialized devices due to gel-induced sediments or obstructions. Seraclean works according to a well established and well known work process.
- In order to achieve reliable test results with the GEL procedure as well, Seraclean may be used as an additional process.
- Seraclean has none of the disadvantages of the GEL procedure: disturbances in the instrumental analysis due to infinitesimal quantities of GEL entering the serum; undesired post-coagulation; the gel is not inert and therefore sensitive to cold.
- Gels absorb large molecules (e.g. medications) which may falsify the test results.
- In contrast to other serum filter procedures Seraclean is very user-friendly and fulfills the highest standards of functionality.

# Expert

**Interview with the specialists Dr. Hanna Engler from Kantonsspital St. Gallen (Institute for Clinical Chemistry and Hematology) and Lukas Bestmann, Head of the Department of General Analytics from the University Hospital of Zurich (Institute for Clinical Chemistry).**

**Can you say a few words about your experience with the gel-based procedure?**

**Dr. Engler:** Separation gels simplify the work process because they create a division – a layer - between the blood clot and the serum/plasma during the centrifugation step. This layer prevents interaction between the cell components and the blood clot. Besides, the serum/plasma layer can be transferred into a tube (which is then used to transport the sample) by means of simple decantation. This is particularly advantageous for samples which have to be sent to the clinical-chemical laboratory by mail.
The disadvantages of separation gel tubes include the fact that some serum samples may post-coagulate after the centrifugation step, and also gel particles may be released occasionally. If the phenomenon remains undetected it may lead to false test results. In extreme cases these gel particles may cause obstructions in the autoanalyzer system, involving significant costs later on. It should also be remembered that separation gels may not be inert. Thus, the analytes contained in the sample

# Opinions

may be re-absorbed. This could lead to falsely low test results and inappropriate clinical decisions.

**Mr. Bestmann:** Gels absorb many large molecules such as medications. The values yielded by the analysis may be 40% below the actual value. This does not happen with a filter system. Such false low values can be dangerous. They may distort the general impression – they would falsely indicate that the patient has very low values of a medication in his/her blood; the doctor may increase the dose and the patient may reach a critically high value (in the worst case this could be in the toxic range). Thus, it will be very difficult to steer pharmacological therapy. Besides, gels create technical problems in special devices such as GC-MS, LC-MS, MALDI-TOF etc. Gels may also interfere with certain ELISA's, clog devices, and lead to costly revisions.

**What, in your opinion, are the advantages of the serum filter procedure?**

**Dr. Engler**: Serum filters serve the same purpose as separation gels. They introduce a barrier between the blood clot and the serum/plasma, which prevents pre-analytical problems due to interactions between cell components and serum/plasma. Thus the original tubes can be used in the analytical devices; this permits positive identification of the sample.
As these serum filters are introduced in the sampling tube after the centrifugation step, it is ensured that post-coagulations and other floating particles are removed from the serum/plasma sample. As serum filters can be used with all types of blood sampling tubes, the pipetting step is not required if the blood sampling tube is used without a separating aid.

**Mr. Bestmann:** Subsequent orders can be made for a longer period of time because the analyses are falsified more slowly. One example is LDH which, in the absence of a filter, is diffused from red blood cells into plasma after a few hours and generates false high values. When a filter is used, the enzyme is withheld and the clinic may send a subsequent order within 12 hours; this could spare the patient the discomfort of additional blood sampling.

**What, in your opinion, are the specific advantages of Seraclean?**

**Dr. Engler:** Seraclean is introduced in the sample container by means of pressure. The long tube allows the filter to be used for every insertion depth. The material is not brittle. Thus, protruding parts of the filter can be cut away so that the original containers of samples with a very high hematocrit content (large percentage of blood cells and relatively low quantity of serum/plasma) can be used directly in the analyzer even after the filter has been introduced. Another advantage is the rounded upper rim and the hole in the upper end. These reduce the risk of injury and the filter can be pushed directly into the container with the thumb because the air is able to escape during the insertion procedure.

**Mr. Bestmann:** Seraclean has no ascending pipe – this makes the filter suitable for the analysis instruments. In devices with an ascending pipe, inexact adjustment may damage pipette needles, and pipette needles are very expensive. As Seraclean is similar to its predecessor, it is easy to handle. Thanks to the long neck of the filter, it can be inserted to the appropriate depth (to the margin of the blood clot) for each sample. The hole at the upper end allows the filter to be pushed downward with the thumb; this causes air to escape during the insertion procedure. Some devices lack this advantage.

**What are your expectations of a product that is part of the instrumentation used for clinical diagnostic procedures?**

**Dr. Engler:** Simplicity, reliability, efficiency, no interaction with analytes or measuring systems, and low extra costs. It would be desirable if the serum filter could be integrated into pre-analytical systems. For instance, automatic insertion and adjustment of the height of the filter in the blood sampling tube. This should occur after the automatized centrifugation step.

**Mr. Bestmann:** Reliability, suitability, simplicity, efficiency – preferably, there should be an automatic system of pressing the filter into the blood withdrawal system.

Dr. Engler and Mr. Bestmann – thank you very much for this interesting and informative interview.

**Dr. Hanna Engler** **Lukas Bestmann**

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# The Cleanest Production by Using the Shortest Routes

*Lars Rominger*




**A new clean-room concept of the medical device manufacturer GEMÜ in Rotkreuz, Switzerland, is based on short routes and thus fewer possibilities for contamination. This concept is based on three important pillars: The first pillar is a special docking system, the second is a series of mobile flow-box systems and the third is a newly developed robot. The aim is to achieve the cleanest possible production process by using the shortest routes.**

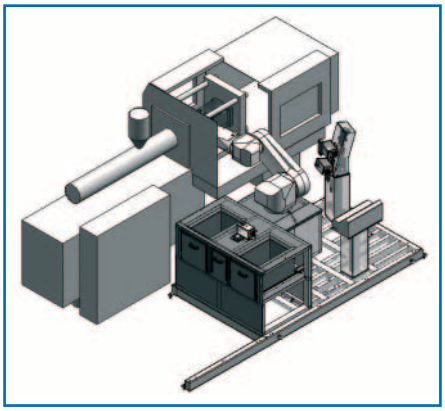
Medicine and medical engineering are constantly making increasing demands on the manufacturers of medical products. Products that are more and more free from contamination are what are required. The most widely established and today the most commonly used status of clean-room technology involves production from the grey room into the clean room itself. This route – from the grey room into the clean room itself – constitutes a not inconsiderable risk of contamination for the products to be manufactured. This process is classified as critical also according to the findings of an EPE (error, possibility and effect) analysis. It was this existing situation that spurred GEMÜ GmbH Switzerland to take action.

## Problem Recognised – Solution Found

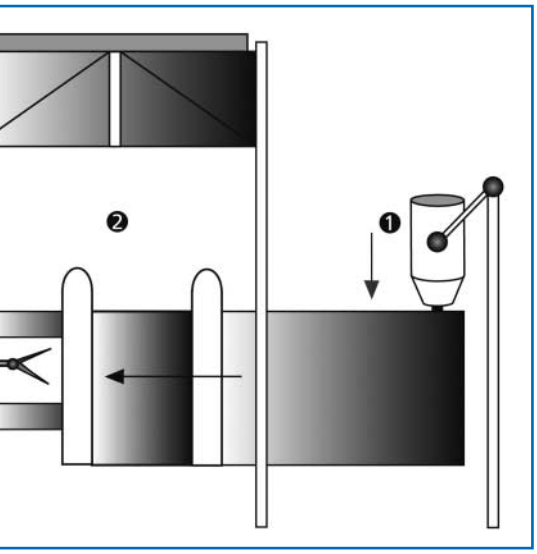
GEMÜ GmbH Switzerland recognised this problem and has developed a new, clear route for the manufacture of plastic medical products. This new, innovative production process is based on three pillars: The first pillar consists of a special docking system, the second is a series of mobile flow-box systems and the third is a newly developed robot (see diagram). Thanks to this clean-room concept, based on using the shortest routes, the Swiss company is in the position to offer the most sterile possible clean-room products.

## New Docking System

The feed-tracks for passing the raw material or granulate into the injection-molding machine should if possible allow no contamination. Today the granulate is often "blown" into the production unit with purified air. In this way the granulate is unnecessarily exposed to the risk of contamination. The solution is "force of gravity". Thanks to a specially developed docking system, at GEMÜ the plastic granulate is released only just before the processing – just before the materiel is melted. This procedure functions thanks to the force of gravity, which delivers the raw material directly to the place where it is to be processed, completely without the use of compressed air.

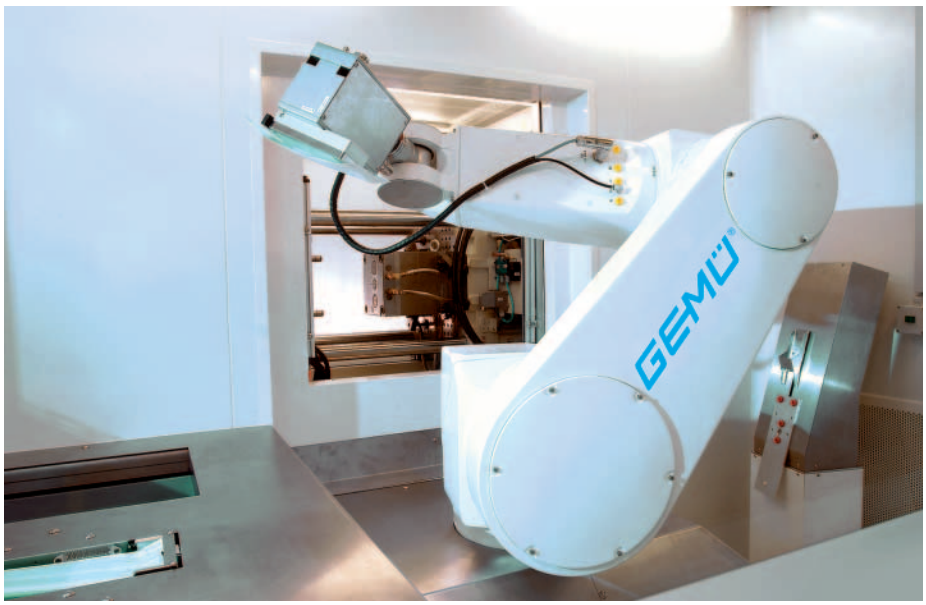


**Robot with injection molding machine in clean room Class 6/7**




**1 Docking system: low-contamination input of granulate**
**2 Flow-box systems guarantee professional island solutions**
**3 The highly-clean demolded plastic components are immediately packed by a specially developed robot under sterile conditions**

**The docking system developed by the company, in practice**




**Clean-room production of GEMÜ GmbH Switzerland, in practice**

## Highest Level of Purity at the Right Place

The second pillar of the production process consists of a mobile flow-box system. By means of these special flow-box systems, "island" solutions are created which are adapted to the different classes of clean rooms. To explain it concisely, this means: All the injection-molding machines are situated in a Class 8 (100 000) clean room and, through the "clapping on" of the flow-box systems, are placed in cleaner conditions. In this way, Class 7 and Class 6 (formerly Class 10 000 and Class 1000) clean-room production conditions, in accordance with DIN EN ISO 14644, can be created. For the assembly, mounting, testing and packing processes, a Class 5 (100) clean room is available at GEMÜ GmbH Switzerland, in which the manufactured products can be subjected to further decontamination.

## Robot for the Shorter Route

The end of the production line for sterile medical products comprises a specially developed robot, which removes the highly sterile injection-molded components directly from the tool at the end of the production process and packs them in sterile bags.

Thanks to these three innovative adaptations, extremely clean production in the clean room can be provided even for particularly difficult and demanding medical products. For example, the clean-room specialist produces plastic components for Verigen AG of Leverkusen, Germany. These plastic components are used, for example, for cartilage transplantations according to the autologous chondrocyte implantation procedure. For this, GEMÜ produces a membrane fixation that is used for the culture of tissue. The tissues obtained in this way are used in the treatment of cartilaginous lesions. As this injection-molded product comes into contact with live cells, an absolutely sterile environment for the production and packing processes is essential. Only in this way it is possible to prevent serious complications.

**About the author:**
Lars Rominger is Head of Marketing/Sales, Medical Engineering, at GEMÜ GmbH Switzerland.

# One-stop Shop in Medical Engineering

*Lars Rominger*

Clean-room production facility of GEMÜ GmbH Switzerland

**Demanding products require special processes. Collaboration between the partners involved, from A to Z, is important. In medical engineering this type of collaboration is particularly appropriate. Process orientation, from the original concept through to the finished product, is what is needed.**

The medical field is still a dynamically growing market of the future. Companies that are active in this field are meeting more and more demanding requirements and are manufacturing ever more sterile and clean products. They do everything possible to ensure medical safety – for the safety of the individual. Today, quite correctly, purity is demanded right down to the molecular structure of a product. Collaboration in this extremely demanding field requires a great deal of mutual trust, and close cooperation is needed – from the original concept to the finished product that can be used in practice.

## System Solutions that Build Confidence

Let us assume that for many years a company has been working successfully in the field of medical engineering, and that now a challenging new problem arises. Many possible ways of solving the problem are considered and thought through. Finally, the possibility is considered of solving the problem with a plastic component manufactured under extremely

### Moldflow Studies

In brief, Moldflow comprises various different types of injection-molding software. The Moldflow production solutions are helpful for better control of the production procedures and increased productivity. These systems allow the planning, equipment, optimisation, control and monitoring the injection-molding process. Moldflow analyses shorten the time required for the development of a new product enormously. Valuable time can thus be saved and the finished product can be introduced onto the market much more quickly. The Moldflow software is available at GEMÜ GmbH Switzerland. This means that Moldflow studies themselves can be carried out.

▶ Further information is available under www.moldflow.com

# Purity your requirement our way of living


**System solutions in plastics for medicine, pharmacy and industry.** GEMÜ Switzerland provides complete system solutions in plastics for the medical device industry and industrial applications ranging from engineering and mold manufacturing, project and quality management, rapid prototyping, mold-flow analysis to injection molding, manufacturing, cleaning, testing, final assembly and packaging, depending on customer requirements – Process-oriented from concept to finished product!

GEMÜ® MEDICAL PLASTICS PROCESSING DIVISION

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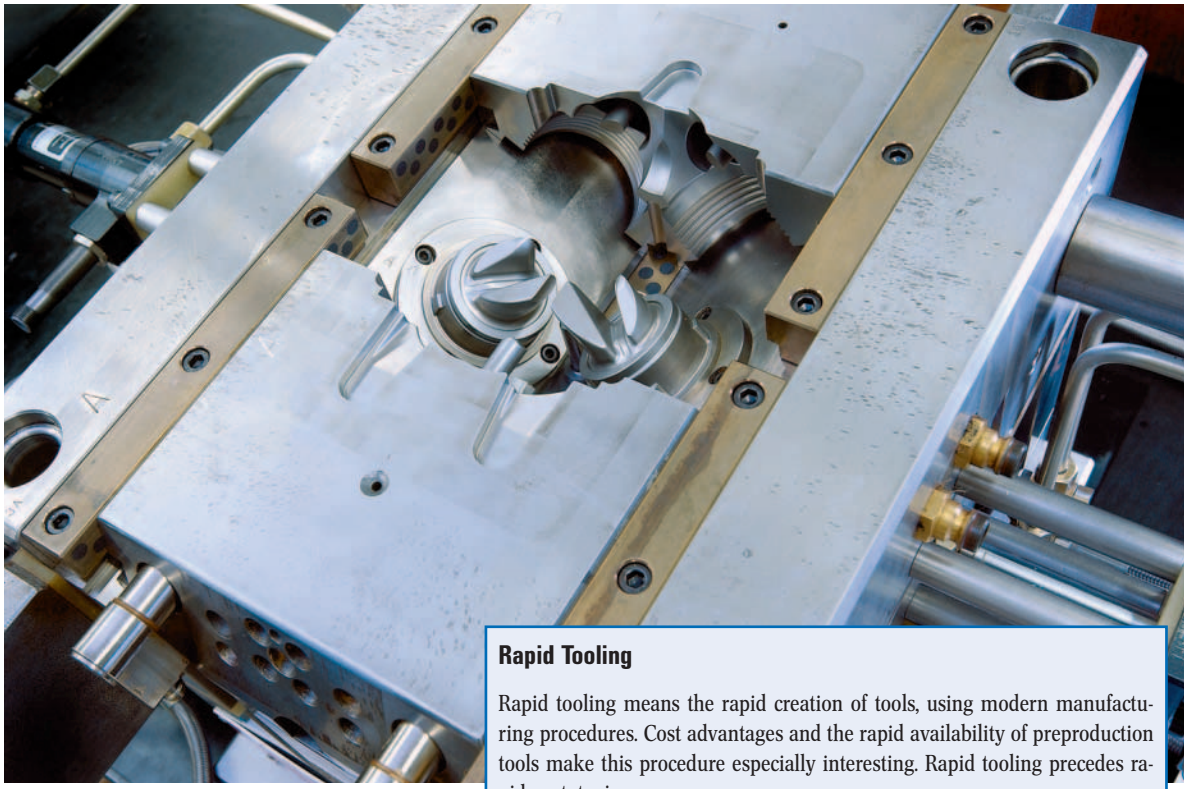


**The right product solution is the one thing, the appropriate tools for the manufacture of the product is the other. Rapid tooling, rapid prototyping and Moldflow all belong to the 1+1 of the plastics engineer.**

### Rapid Tooling

Rapid tooling means the rapid creation of tools, using modern manufacturing procedures. Cost advantages and the rapid availability of preproduction tools make this procedure especially interesting. Rapid tooling precedes rapid prototyping.

### Rapid Prototyping

Rapid prototyping comprises various different rapid process procedures for the manufacture of prototypes, which are manufactured under series-like conditions.

After the rapid tooling and rapid prototyping processes serial-produced tool and the serial-manufactured product are available. Thanks to the rapid tooling and rapid prototyping, the development costs can be lowered and the development times shortened, in comparison with the conventional methods. The shorter development times in turn allow more rapid introduction onto the market, which in the present market environment is extremely important.

sterile conditions. In this case an appropriate one-system solution is already available – a solution which is carried out, from the design, through functional project management and quality management, to the production and assembly of the product, by one company. A one-system solution has many advantages. Thanks to the close collaboration and the different feedback channels, direct contact between the partners in the project is maintained at all times. Confidence and mutual understanding of the problems to be solved are built up, as well as mutual know-how. Collaboration of this type results in a considerable saving of time, which should not be underestimated. For example, problems have to be explained only once, so that the lines of communication are shortened enormously.

## From A to Z

The procedure for a one-system solution is simple. Already in the course of the first discussion with the customer the plastics engineers present their initial ideas for solving the problem. They then set about drawing up possible designs and producing the first prototypes. Here, Moldflow analyses, rapid tooling and rapid prototyping are all part of the ABC of the plastics engineers. Only in this way the time to market can be kept short and very considerable savings be made in the development costs, compared with the old procedure.

## https for Reliable Communication

Regular contact with the customer is also important. This allows the customer to continually follow the different intermediate steps right through to the final solution of the problem, and to give his input. In the final analysis it is the customer who decides which solution is to be adopted. In this connection, personal discussion is immensely important. Also ideal, however, is a digital solution, via an Extranet. Each person involved in the project has a password, and in this way can have access to, and can work on all the data relating to the project. By means of https, all the information is protected against unauthorised access. While a document is being processed, no other person can work on it. As soon as the document has been released again the changes that have been made can be seen by all the project-members. In this way all the persons involved can always see the present status of the project.

GEMÜ Switzerland offers a modern system solution, is a partner of the company Moldfow, has its own tool-making department and a secure https Extranet, with which everything can in fact be kept under control, from the first step to the last. Changes and adjustments that may be made in order to improve the quality of the product are also possible at any time. Rapid tooling and rapid prototyping are also part of the procedure.

## The Most Modern Production Facility

If a company wants to keep pace with the latest technologies, it must have the most modern pro-

**The finished products are packaged under clean-room conditions of Class 5 (100).**

duction facilities at its disposal. Particularly in the fields of medical engineering, pharmaceutical technology and biotechnology, regular investment in machinery and equipment is essential. In order to be able to manufacture products for use in highly clean and sterile applications, the appropriate clean-room production facilities must be available. Today, clean-room production conditions of at least Classes 8, 7, 6 and 5 according to DIN EN ISO 14644 have to be adhered to.

For sterile production from A to Z, the final stages of the work must not be forgotten. Here the same quality criteria apply as for the production process itself. The concluding stages include the professional decontamination, the assembly and fitting, the various testing and checking procedures and packing of the product under clean- room conditions. Also for the packing in the clean room, the partner company should meet the requirements of Class 5 in accordance with DIN EN ISO 14644 (100).

**Final control: Each product is carefully checked.**

### Good Manufacturing Practice (GMP)

GMP is a prescribed procedure for the manufacture of products in accordance with the latest state of science and technology. The aim is the manufacture of drugs of consistently high quality – for the safety of the patients. GMP meets this challenge totally. The quality assurance system covers not only the manufacturer's own personnel, but also that of its suppliers and marketing firms. The GMP procedure issues instructions in regard to staff training, manufacturing premises, process documentation, production and quality control, as well as self-inspection and inspection by outside agencies.

At the beginning of their activity for the company, and also regularly thereafter, all employees must receive the appropriate training. This training and further training covers not only the handling of the equipment but also the necessary health and hygiene requirements and instructions. So that the risk of errors can be minimised and thorough, unproblematical cleaning and maintenance can be made possible, the premises and the facilities must be installed accordingly. Also, clearly written documentation is essential. This prevents the errors and misunderstandings that may result from verbal communication and also allows a particular production batch to be traced back to its origin.

A system of quality control that is independent of production must be involved in all decisions concerning the quality of the products. All objections (internal or external) regarding possibly defective products must be carefully checked according to procedures that are laid down in writing. Also, systematic steps must be taken so that defective products can be quickly withdrawn from the market.

### Important Quality Control

In the production of medical components QUALITY has to be written large, because in the final analysis lives may perhaps depend on these highly sterile, clean components. At GEMÜ GmbH Switzerland, for example all the processes and the products are checked and validated regularly. The ISO 9000 series has long been adhered to and constantly controlled. At GEMÜ all the production stages meet the standards set by the FDA (Food and Drug Administration and also conform to the EG GMP guideline (Good Manufacturing Practice).

**About the author:**
Lars Rominger is Head of Marketing/Sales, Medical Engineering, at GEMÜ GmbH Switzerland.

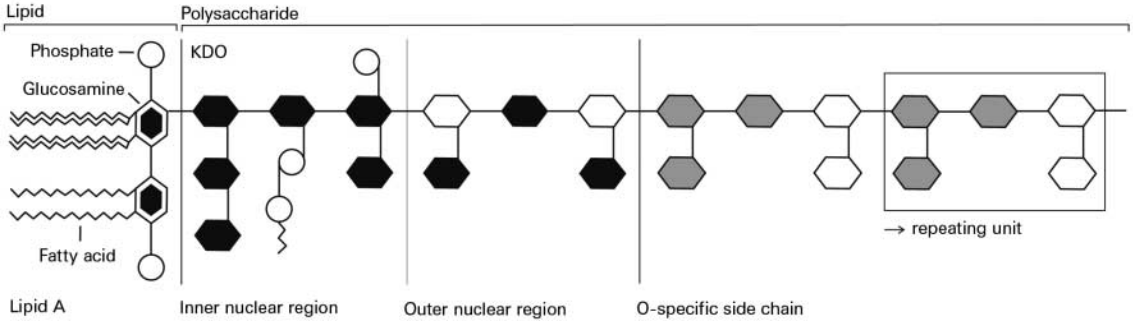
# Endotoxins – the Underestimated Danger

*Lars Rominger, Dr. Frank Stieneker*

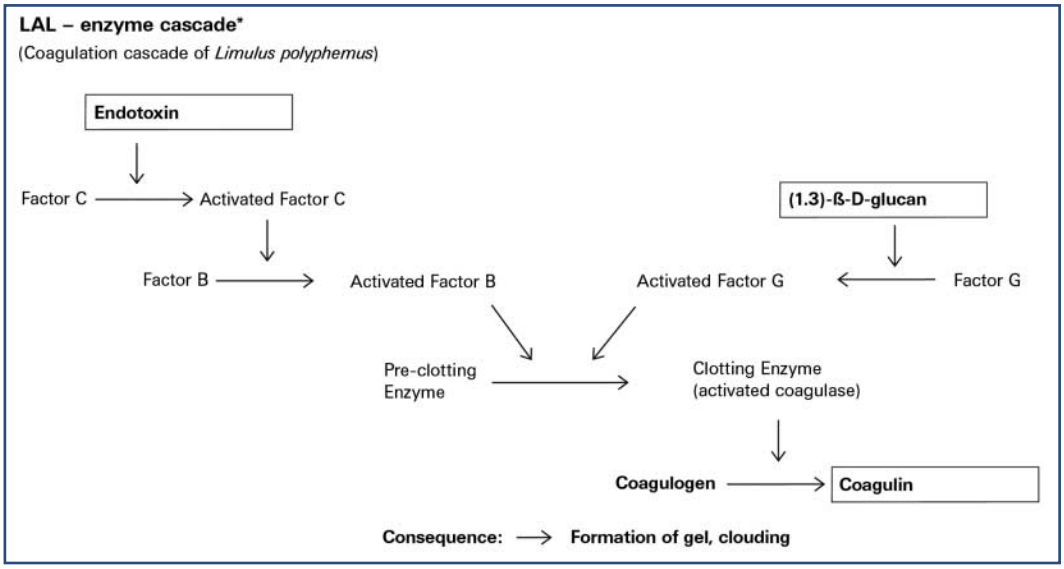
**A Limulus polyphemus in its natural environment**
(Photo: Dr. Rainer Scheer, Pforzheim)

**Endotoxins are omnipresent. Their effect on the human body is dependent on various different factors – but under certain circumstances they can in fact be fatal. However, up till now too little attention has been paid to endotoxins in the field of medical engineering. It is important that the products are kept free from endotoxins. An aseptic working procedure, with low particle content, is a precondition for the manufacture of endotoxin-free medical products, but this alone is not enough. Here new measures are demanded, for the safety of the patients!**

**Structure of a lipopolysaccharide***
(Rietschel and Brade, 1982)




* The diagrams and illustration were kindly made available to us by the Pyroquant Diagnostik GmbH. This firm is a leader in the field of endotoxin and glucan determination. Pyroquant Diagnostik GmbH markets in Germany, and also in Switzerland, all the reagents, equipment and laboratory aids for the detection of endotoxins and (1-3)-ß-D-glucans.




Endotoxins are toxins that are produced by gram-negative bacteria. Unlike ectotoxins, they are not excreted from the body but remain in the cells, and especially on the surface of the cells. They are thermostable and are bound to the cellular substance of the microorganisms, and are therefore only released at the moment of cell death. The effect of the endotoxins is mostly immunogenic. They are neutralised by antisera less effectively than ectotoxins. Biochemically they are lipo-polysaccharides (LPS), which are composed of different species-specific polysaccharide chains and a relatively uniform lipid (lipid A) (see diagrams). The terms "endotoxin" and "lipopolysaccharide" are therefore often used as synonyms. The toxic property of the endotoxins is determined by the lipid A. Its activity is, however, modified by the polyssaccharide portion.

## Omnipresent in the Environment

Gram-negative bacteria are to be found everywhere. They accompany us throughout our whole life. They are a natural substance and occur in different concentrations everywhere in our environment, for example at home, in the agricultural evironment and in different industries. They colonise the human skin and the intestines, are adsorbed onto particles in the air and are also to be found in water. The sterilisation of articles or of water leads to the death of these bacteria, and thus to the release of the endotoxins. The endotoxins themselves are well adsorbed by different surfaces and are then released from the bonding site by competitive displacement.

## Pulmonary Problems with High Endotoxin Levels

As a rule, the time and the amount of the exposure to endotoxins are the factors that determine whether they will lead to health problems. In certain workplaces the concentration of endotoxins present can be high. High endotoxin levels are to be found, for example, at some workplaces in the agricultural sector, in the cotton-processing industry, in chicken slaughterhouses or in the metal-processing industries. The connection between endotoxin levels and changes in the pulmonary function in persons working in the cotton industry has been known for a long time and has also been investigated.

## Different Effects

Endotoxins can have different effects, depending on different factors. On the one hand, the portal of entry or the site of action and the concentration, for example, can play an important role. On the other hand, the predisposition of the person concerned is responsible for the different effects in the organism.

When working in an environment with high endotoxin levels, these are inhaled through the airways. Acute inhalation of endotoxins can cause coughing, impair the pulmonary function and lead to influenza-like symptoms. Long-term exposure can lead to chronic bronchitis.

## Microbial Intoxication

In the case of a parenteral intoxication (through the blood stream), the effect of the endotoxins is more rapid and more severe. If endotoxins pass directly into the organism, for example in the course of a surgical intervention, they have a systemic effect. They lead to sudden high fever. Only very small amounts in the blood stream are sufficient to cause fever. For the safety of the patients it is therefore particularly important to work with medical products that are free from endotoxins. Purity down to the smallest detail is what is required. This applies especially for implantable medical products, or for medical products that come into contact with implants. Adjuvants that are contaminated with endotoxins and are then used in cell cultures can also have negative effects on the cell growth, and after the implantation of autologous cells in the body can cause effects on the tolerability.

## The Danger is Known

Simply through contact with a person, through his breath, through the air or through water (even purified), endotoxins can get onto the surface of medical products. Certain metals often have a bactericidal effect and are not an ideal surface for the colonisation of bacteria – in absolute contrast to plastic materials. Here it is therefore particularly important to work prudently. Although working in an aseptic, particle-free environment is a prerequisite for the manufacture of medical products that are free from endotoxins, this is in fact not sufficient, because:

- sterile does not automatically mean endotoxin-free;
- particle-free does not automatically mean endotoxin-free.

For endotoxin-free products, the microorganisms that are present must not only be killed, but must also be removed. Simple disinfection is therefore not sufficient. GEMÜ GmbH makes great efforts to ensure that no gram-negative bacteria find their way into production process for medical products. Clean-room conditions, similar to those applied for the manufacture of parenterally administered drugs, will be implemented in the future. If no gram-negative germs can be detected in the raw materials or in the prodution process, then there will also be no endotoxins on the end-products. The presence of endotoxins is detected specifically by means of the LAL test (LAL enzyme cascade, see Diagram). The detection limit lies in the nanogram/ml range. Thanks to these efforts, in future not only endotoxin-free metals will be used in the medical field, but also endotoxin-free plastic components – for the safety of the patients.

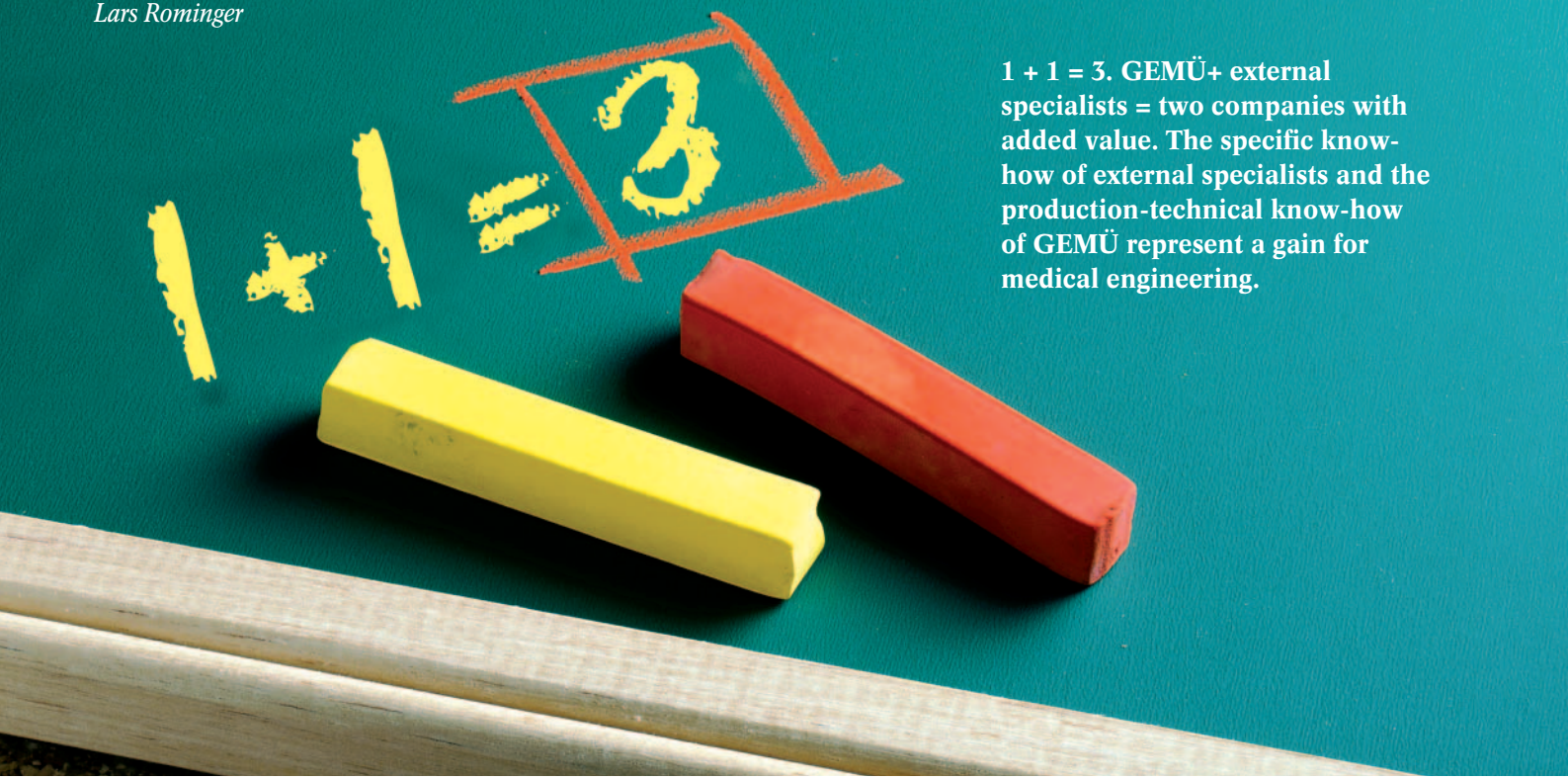
**About the authors:**

Dr. Frank Stieneker is Head of the Business Unit of the Working Association for Pharmaceutical Procedural Technology (AVP) in Mainz. At the same time he is a Lecturer in Pharmaceutical Technology at the University of Frankfurt.

Lars Rominger is Head of Marketing/Sales, Medical Engineering, at GEMÜ GmbH Switzerland.

# Two Companies One Aim – Satisfied Customers

*Lars Rominger*



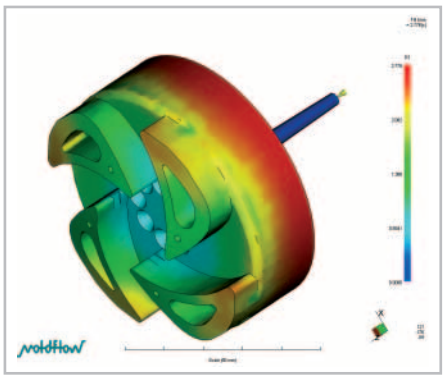

**1 + 1 = 3. GEMÜ+ external specialists = two companies with added value. The specific know-how of external specialists and the production-technical know-how of GEMÜ represent a gain for medical engineering.**

## 1+1= 3 the Example Dyne is Illustrating it:

Clemens Dransfeld, the Managing Director of Dyne, founded the firm in 1995. "Now almost ten years ago, I became aware of the lack of a competent service provider in the field of structural plastics and composites", Clemens Dransfeld explains when describing the beginnings of his company. This gap is now filled by Dyne, who offer comprehensive services in the planning and development of components from reinforced plastics and high-performance composites. The corporate philosophy is simple and is quickly explained: "Creativity and innovation are important elements for successful product development" is how the Managing Director describes it. This philosophy is put into practice and the firm's success certainly justifies what Clemens Dransfeld says.

## Delighted with the Alinghi Team

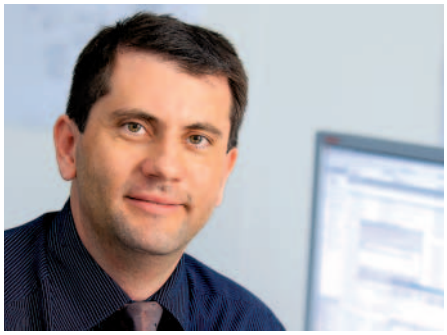
Thanks to its interdisciplinary composition, the four-person team from Dyne has already won several awards for industrial design. Last year, for example, Dyne won the iF Design Award for their contribution to the development of an implant. The iF Design Award is one of the most important design competitions in the world and every year it receives more than 1800 entries from 30 countries. "A particular highlight was our collaboration in the design team for the Americas Cup yacht, Alinghi", says a delighted Clemens Dransfield. "We were emotionally involved in each race and were absolutely delighted with the success of the Swiss yacht."




**Mold Flow analysis**

## Successful Collaboration

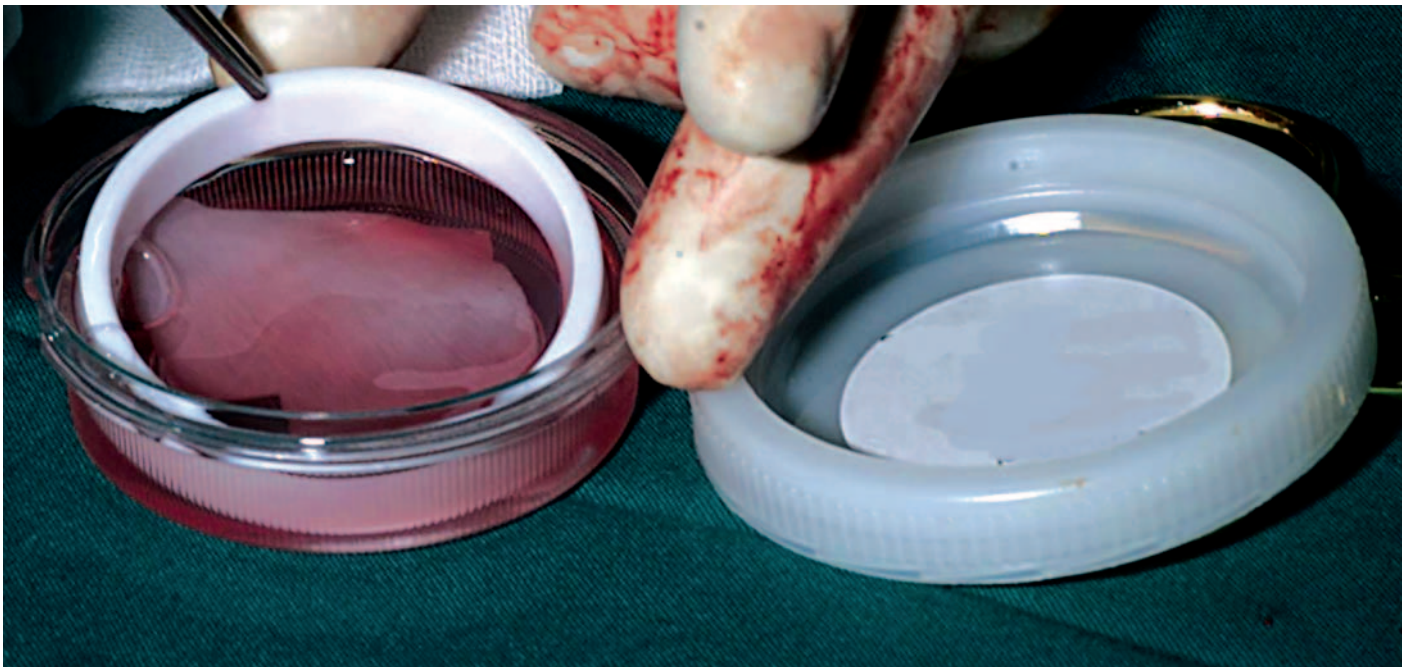
For several years, Dyne has been working with GEMÜ. Many projects have already been completed and the innovative products are already on the market and have proved their value in practice extremely well. Clemens Dransfeld and René Fischer, the Project Engineer, are very satisfied with this collaboration. "Within a very short time GEMÜ has built up outstanding competence in the field of medical engineering. With the provision of the clean-room conditions, the engineering and their own tool-making facility, at GEMÜ we receive everything from one place", says René Fischer. "We are very satisfied with this collaboration. At GEMÜ we are receiving very good advice, and the time-frames that are set are always met", says Clemens Dransfeld, who is also delighted with the successful partnership. Dyne and GEMÜ complement one another ideally. With this terrific collaboration, one-plus-one doesn't make two, but three!



**About the author:**
Lars Rominger is Head of Marketing/Sales, Medical Engineering, at GEMÜ GmbH Switzerland.

# A Difficult Project Successfully Completed in a Very Short Time

*Philipp Bächtold*



This plastic component comes into contact with live cells and it must therefore be possible to produce it as germ-free as possible and to use it under sterile conditions. GEMÜ GmbH Switzerland solved this problem and drew up the necessary documentation within just four months.

**A new manufacturing process for a medical product was developed at GEMÜ GmbH Switzerland within a period of only four months. In this connection the standards of Good Manufacturing Practice (GMP) and the conditions of the Swiss Law on Drugs had to be adhered to.**

Time is money – also in the field of medical engineering. In order to be successful, product innovations have to be brought onto the market as rapidly as possible. In mid-September 2003 Dr. Wilfried Wächter, Head of Manufacturing and International Production Manager of Verigen, approached Lars Rominger, Head of Medical Engineering Marketing/Sales at GEMÜ GmbH Switzerland, with a problem. Wilfried Wächter had to renew a medical component needed in the manufacturing process for matrix-induced autologous chondrocyte implantation (MACI®). The defaults for Lars Rominger were clear: a sample of the plastic component was already available, but not the manufacturing procedure in accordance with GMP and the corresponding documentation. The latter is urgently required by the supervising authority, for the sales of the "biological drug". Both have to be provided as quickly as possible.

## Problems Solved in Record Time

The plastic component has now already been in use successfully since the end of January 2004. "Their experience in the manufacture of plastic materials and the availability of appropriate modern facilities for the provision of clean rooms convinced us that we should enter into collaboration with GEMÜ", explained Wilfried Wächter." This collaboration was simply fantastic", he continued. "I never thought that this complex procedure would be made available – together with the complete documentation – in such a short time". The complete, correct documentation was particularly important for the approval by the drug regulatory authority.

## Verigen: a High-tech Company

Verigen AG is a production company active in the field of medical biotechnology. This company, which was founded in 1999, has its Headquarters in Leverkusen, Germany, and has further production units in Denmark and Australia. It offers, among other things, the matrix-induced autologous chondrocyte implantation – MACI® for short. This international company has its core competences in the field of tissue engineering for orthopaedic therapy and has about 80 employees worldwide. For further information on the company and its therapeutic methods, visit its website, www.verigen.com.

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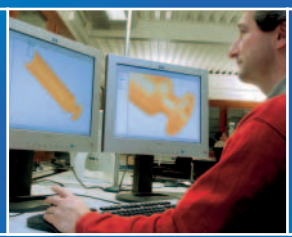


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