

PNS Professional Nutrition Services

TRANSPARENT QUALITY





Dear Readers,

Anyone seeking to improve people's health must examine the tasks at hand and meet them head on. At B. Braun, we approach this challenge with our guiding principle of "Sharing Expertise." To us, it means developing effective solutions for the healthcare industry that protect and improve the lives of people around the world, through constructive dialog with our customers and partners.

The opening of the B. Braun subsidiary PNS (Professional Nutrition Services GmbH) is a successful example of how we not only embody "Sharing Expertise" with our customers and colleagues, but have also infused this guiding principle into the creation process of our new location in Melsungen. In close collaboration with our construction and project partners, we have developed a new production facility for patient-customized nutrition solutions that meets the latest standards of technology and quality. This applies not only to the production equipment, but also to the building design and materials. PNS manufactures according to strict GMP guidelines and with the maximum standards for clean room conditions, allowing our patients to be cared for safely.

The planning of the new production facility also sets standards for a possible expansion of our business – including internationally. From the dimensions of the manufacturing process, we will also be able to build such a production facility at other locations in the future, transferring the production processes one for one, like a blueprint. It's a great example of how we have been able to create innovations and more efficient processes during this new construction which are becoming standards.

PNS stands for the highest technical level and tailor-made services with high quality products. The new production facility is therefore a successful investment not only in the region, but also for the future of customized patient medical care.

Otto Philipp Braun

Member of the Management Board of B. Braun Melsungen AG



Model for the future: Clear architecture, an optimized production process and modular expandability characterize the new construction of B. Braun's compounding plant in Melsungen.





Dear Readers,

After just twelve months, we are commencing operations at our new PNS (Professional Nutrition Services) production facility. It is a modern production plant at the Melsungen location which meets the latest technological requirements and the highest quality standards.

I am very pleased that we have been able to make this construction project a reality, despite the tight schedule, and within the planned budget and quality framework. It is an accomplishment that we have achieved through exceptional cooperation with the construction and project partners. I would like to take this opportunity to offer my thanks once again to all of those involved.

Outstanding performance and quality are also unified in the products that are manufactured in this modern production facility, in a kind of workshop environment: patient-customized nutrition solutions for parenteral use, or so-called "compounding." These products make an important contribution to the clinical nutrition of patients who have very specific requirements and cannot be adequately cared for with standard products.

Because PNS produces the nutrition solutions aseptically, the highest demands are placed on the clean room conditions. That's why half of the overall seven million euro investment went into the clean room equipment.

As a result, we are ideally positioned: we can meet the rising demand for such services and, together with our employees, we look forward to impressing our customers and partners with the maximum standards for quality and safety in individualized patient care.

Oliver Eichhorn CEO, Professional Nutrition Services GmbH

Enough energy, every day

The production of parenteral nutrition solutions places the highest demands on technology and quality.



For critically ill, malnourished patients, customized nutrition solutions are life-saving in many cases. Parenteral nutrition is always a step toward improving their quality of life.

When people are no longer able to obtain sufficient nutrients and energy from a normal diet, their lives are threatened over the long term.

The reasons for illness-related malnourishment are diverse and require appropriate and systematic nutrition therapy. Various forms of nutrition therapy can be used: oral, enteral, parenteral.

B. Braun offers a complete line of products for this purpose: Nutricomp[®] sip and tube feeding for oral and enteral nutrition therapy, NuTRIflex[®], NuTRIflex[®] Lipid and NuTRIflex[®] Omega for standardized parenteral nutrition, and then, supplemental to this product line, patient-customized compounding for parenteral nutrition in nearly every therapeutic situation.

What's more, we also support all people involved in the care of critically ill patients, with professional advice and solution-oriented services. For example, B. Braun employees can take over the coordination of a reliable, in-home parenteral nutrition therapy when the indication for parenteral nutrition continues for patients after a hospital stay. Patient-customized compounding refers to the mixing of base nutrient solutions (amino acids, glucose, lipids, electrolytes) in quantities that are precisely tailored to the very specific needs of individual patients. These specific needs typically arise in patients with short bowel syndrome, children, patients with diabetes or liver dysfunctions and in the case of dietary supplementation for dialysis.

Sensitive base nutrient solutions must be mixed under sterile conditions and with continuous monitoring. These products are medicinal products and meet all requirements placed on drug quality.

Following a precise requirements calculation, an individualized parenteral diet is prescribed by a doctor.

The pharmacy, which is not normally equipped to produce this diet itself, contracts PNS Professional Nutrition Services GmbH with the manufacturing. The products are delivered refrigerated, with a maximum lead time of two days.



Professor Dr. med. Arved Weimann, Chief Physician at the Clinic for General and Abdominal Surgery with Clinical Nutrition Department of the St. Georg Hospital in Leipzig since 1999.

For which patients is parenteral nutrition even a consideration?

Professor Dr. med. Arved Weimann: The indication for total parenteral nutrition (TPN) is generally rare – nutrition can usually be a combination of oral/enteral/parenteral. In oncology, it can apply to certain cases of peritoneal carcinomatosis. The updated DGEM guidelines say: "Long-term artificial nutrition should be performed as ambulant enteral or parenteral nutrition in the case of relevant chronic restriction of food intake or absorption." In the case of parenteral nutrition, the oral and enteral intake options, including intensive dietary consulting in an incremental regime, have truly been exhausted. This applies when no more than 60 to 75 percent of the patient's energy needs can be absorbed through

oral/enteral means. Of course, this must be discussed and coordinated with the patient on a very individual basis. In the case of malnourished patients who require dialysis, the dialysis can be used for parenteral nutrition.

Quality of life, compliance, safety: what is the most important aspect of nutrition therapy?

All aspects are important, of course. Quality of life is a crucial therapeutic goal, while patient compliance is absolutely necessary in order to avoid complications. Safety is only feasible in an informed environment which involves not only the patient and their family, but also the family doctor, private nutritional medicine practitioners and especially nursing services, as well as the home care provider. Because infectious catheter complications are a primary problem, a connection with a clinical outpatient nutrition department with background experience in infectiology is required for management of complications.

A person receives parenteral nutrition at home. Do the necessary structures exist in Germany for nationwide care?

Discharge management and transitioning from the hospital to artificial in-home nutrition with professional care provided by a "home care service" are established nearly nationwide in Germany. Generally binding and transparent standards of quality are in development and are, in my opinion, urgently required.



"Quality requires transparent and robust processes." Dr. Martin Klingmüller Quality Manager, PNS Sub-Project Manager, Process Technology

A workshop with exemplary character is created

Success through competence and "Sharing Expertise"



"There can be no compromises when manufacturing medications. Together with our partners, we have created an innovative location that unifies quality, safety and transparency." Jens Kann Project Manager Global Process Engineering, B. Braun Melsungen AG



Success through competence and "Sharing Expertise"

B. Braun has been operating a compounding service together with PNS Professional Nutrition Services GmbH (PNS) in Melsungen since 2003, which expands the company's product portfolio with custom-produced parenteral nutrition. A clean room system according to EU-GMP regulations is a requirement for the aseptic manufacturing of these medications. It is a production standard which places the highest demands on technology, processes and personnel.

After more than ten years of consistent production at the old location, an update to the current state of technology and an advancement and optimization of the production processes became necessary. In July of 2014, B. Braun Melsungen AG therefore decided to construct new production facilities. An internal B. Braun team took over project management in 2014 and was responsible for the design, implementation and management of the new building. The new PNS plant was to conform to the B. Braun guidelines architecturally, and to implement everything technically feasible in compounding.

Lots of glass, for a complete look into all production areas. The architectural concept is the consistent implementation of the corporate design

Right from the start of planning, the construction design process involved dialog with international colleagues in Great Britain, Ireland, Italy, Poland, Spain and the USA. Ideas, suggestions and previous experiences from already completed compounding production facilities were exchanged, and "Sharing Expertise," the guiding principle of the company, was put into practice.

One technical innovation developed by the exchange of experience, for example, is the development of a refrigerated material lock, which simplifies the manufacturing process and even better guarantees the compliance of the refrigeration chain.

Corporate design in all areas

Characteristic B. Braun style elements are incorporated into the design of the entire production facility.

The architecture and clean room concept of the new production facilities meet the highest standards and have groundbreaking character

The building itself assumes the design vocabulary of the company and follows the specified architectural patterns. It has recognition value as a B. Braun plant. That which has already been constructed in the "large" LIFE plants is reflected here on a smaller scale: the same colors and materials, the same transparency concept, the same material quality. The entire building is designed as a simple cube, with lots of light and an open configuration.

The new production facility is also intended to serve as an implementation study for other compounding locations. It shows that the concept can be successfully transferred with respect to transparency, modularity, quality and sustainability.

The visitor area is one example of PNS's transparent design: without disrupting operating procedures,

customers and interested parties can view the production directly through a glass visitor's hallway, following each manufacturing step and seeing the high production standards for themselves.

The modularity is intended to facilitate reproduction of the system: the building geometry and configuration have been chosen so that implementation in other countries can also be achieved cost-effectively. Of course, a modular expansion to the current project with an additional production space is possible without interrupting ongoing operations.

The production area must ensure sterility for the production. Germs and particles must remain outside.

For that reason, the interior construction of the production facility is structured according to an "onion skin principle." This partitioning separates the work areas from each other, preventing contaminants from being carried over into cleaner areas. Personnel and material locks connect the clean room zones.

The office spaces, the materials warehouse, the restrooms, the building technology and the visitor hallway are in the "black area," or less controlled area, at PNS. The production and quality control departments are in the "white" area. Further cleanliness stages, from GMP class D to class A, are then implemented within the "white" area.







The corporate design is also continued in the interior.

Creating quality

A pure process – from the order to the patient.

The production process of a nutrition solution begins with the individual prescription for a patient, which the pharmacy forwards to PNS. Following examination of the formula, production begins with the assembly of the initial products, which primarily originate from B. Braun's internal production.

From the warehouse, the initial products enter pre-disinfection via a material lock, then enter disinfection and finally find their way into the GMP Class B production area, through a specially developed, particularly wide pass-through lock. The personnel enters the production area through a multi-stage lock. There, the computer-controlled filling machines are located in the clean workbenches.

The disinfected initial products are connected to the machines and filled into sterile bags according to the formula. The bag is then sealed, germ-proof, and removed from the production area through a second material passage. Each finished bag is then inspected, labeled and sealed in a film bag. Systematic quality inspections provide verification of correct dosing and sterility. The nutrition solution is then stored overnight in the refrigerated passage.

The next day, the compounding products are shipped by express delivery to the pharmacy, in specially certified refrigeration boxes.





Formula: formula control and interface to control software



Lab: daily chemical in-process controls to ensure performance.





Personnel locks: clean separation of the clothes-changing process.



Visual inspection, labeling and refrigerating: visual inspection of finished products, storage in the refrigerated locks.



Disinfection: all initial materials must also be germ-free on the outside.



Production area: filling under maximum product protection.

Collaborative design

Openness and transparency practiced in all planning phases.



The glass visitor's hallway provides direct views into the entire production process.

Very different demands are placed on "black" and "white" areas: in the "black" area, for example, the construction of which is primarily managed by the company Baudienstleistungen Vogt, workmanship and the corporate design of the interior play an important role.

Stylistic architectural B. Braun elements that

are already used in the Group's LIFE plants can also be found in the "black" area of the production facility. For example, the vestibule, foyer, hallway and restrooms feature the characteristic exposed concrete walls. In the administrative area, with office spaces and a conference room, carpeted floors, wood-glass partitions and office furniture create a familiar picture. In the



The entire production facility was planned by B. Braun Engineering and implemented in coordination with the contributing project partners.

employee areas, such as the break room and changing rooms, one finds the characteristic B. Braun red coffee kitchen line and the light blue lockers with dark blue counter bench.

A proven concept, but with innovations

The characteristic B. Braun architectural design of the interior doesn't stand in the way of advancement.

One innovative change that the B. Braun project team developed together with the companies Syring and Bayer Vitrotechnik are the specially produced glass partition walls in the general office area. These glass-wood partitions have advantages over previous designs, in that they are easier to clean and absorb more sound The flush-mounted glass, made from a nearly ten centimeter thick, soundproof laminated glass pane, allows no contaminants to penetrate into the intermediate space, which contributes to a more finished design and reduced maintenance efforts and costs.

Another highlight is the steel technology platform on the top floor, which was installed by the company Metallbau Singer. The staging makes a cost-intensive suspended ceiling unnecessary in the building. All ventilation and air conditioning components and all control cabinets for CR monitoring, instrumentation & control technology, electrical sub-distribution and IT network cabinets are optimally accessible here for operation and maintenance. The clean room ceiling is also designed to be accessible; all volumet-

Optimal, collaborative technology planning

Planning of the technical building services equipment entrusted to PG Schnepft.



In order to facilitate operation and maintenance, a separate level was provided for the complex technology, and also designed with transparency. Everything is controlled and serviced from here, without having to enter the clean room.

ric flow controllers for the ventilation technology and other technical equipment can always be easily and conveniently reached. This allows work in the clean room to continue uninterrupted in case of a service call.

A clear view and quality are essential in the clean room

The production space is the heart of the PNS production facility. The standards of cleanliness, transparency, quality and reliability are the highest here.

At PNS, the desire for transparency is met by a maximum proportion of glass in the interior design. Eye contact between employees is essential for smooth communication and a high standard of work safety in production. Thus there is a clear view in the clean room, from pre-disinfection, through the production area, to finished product testing.

Once underway, the compounding operation cannot be interrupted for an extended maintenance period. As a result, the quality and durability of the necessary technology must be accounted for from the beginning. This requires placing maximum focus on material and device selection, process optimization and perfect assembly, right from the start. With the company IB Wiegand from Kassel, B. Braun was able to gain a well-known and reliable partner that guaranteed constant, professional monitoring of the clean room construction and compliance with the schedule. The PVC floor is also a critical design factor in the clean room area. Heavy mechanical stress and frequent disinfection require good adhesion and seamless jointing. The company Komplett Bau Nuredini brought many years of experience in clean room floor construction, technical expertise and high quality workmanship to the project.

Creating innovations through trust – B. Braun relies on regional partners

Of course, other partners were also needed for the planning and implementation of such a project, which were found in the engineering firms PPC Projekt-Planung & Consulting GmbH and PG Schnepf. PPC executed the architectural design of the building, while PG Schnepf was responsible for the technical building equipment.

Long-standing and experienced project partners of the company were called upon when selecting project partners, in order to successfully achieve a fast-paced realization of the construction project. These companies are locally based, such as Tresolid or Haustechnik Melsungen, but companies such as Neuberger Geräteautomation GmbH or Vitec were also involved.

In this environment of partnership and collaboration, the construction project, with the high standards of quality it placed on clean room technology and interior design, was successfully completed with a small steering team within the scheduled construction period of only twelve months.

PG Schnepf

For the planning of the entire technical building equipment (TBE), including clean room ventilation, the developers relied on the expertise of Schnepf Planungsgruppe Energietechnik GmbH & Co. KG, from Nagold. Collaboration with this company, which operates in all areas of building services, had already proven effective many times over since 2001, in various B. Braun Melsungen AG projects. Specifically, they took over responsibility for the technical planning and construction supervision of the ventilation, heating, refrigeration, plumbing, electrical engineering, fire alarm systems, IT network, building automation and ventilation control in this new construction.

User-friendly and reliable

Neuberger combines modern GMP monitoring with intelligent building control technology to form a homogeneous system.



Expert installation and easy operability of clean room monitoring.

Before starting the technical implementation phase, the production process and system layout were defined. This information was supplied by the core design team from B. Braun Melsungen AG.

PG Schnepf gave the subsequent technical implementation planning high priority. All technical disciplines with responsibility for construction and TBE were involved from the start, along with the later operators of the production. The contracted companies could also be integrated in an early project phase, thanks to a timely bid process. This procedure enabled optimal coordination of execution dates and construction processes and led to a smooth construction process.

The TBE design experts paid particular attention to the 63 square meter, hygiene classification B production area, with a spatial volume of 200 cubic meters. Special ventilation technology was designed here which enables nearly ideal air distribution in the space.

The hygienic zone and pressure stage concept is prerequisite for later successful hygienic work. The technology must permanently guarantee the required room pressure differences between rooms of different cleanliness classes. The cleanest room has the highest air pressure and must be supplied with air that is nearly completely free of germs and dust.

Neuberger

The design of a powerful clean room monitoring system (CRMS) in collaboration with the implementing company Neuberger ensures that the parameters relevant for all clean rooms, such as airborne particles, room air pressure and temperature, are permanently measured and ultimately complied with.

Neuberger has already successfully collaborated for many years at numerous B. Braun locations. It is a specialist in monitoring systems and high-tech building control technology. Together with B. Braun and Schnepf, Neuberger planned and designed an integrated automation system in advance for monitoring and building technology.

The system structure is both efficient and safe; the installed sensors are used both for monitoring as well as for regulation and control of the building services technology. This eliminates duplicate instrumentation, which has a noticeable effect on investment costs and consequential costs, such as for regular calibration. A positive side effect is that there are no deviations between the recorded measured values for GMP monitoring and the control.

Flexibility and commitment

Professional clean room ventilation technology from HM Haustechnik Melsungen.



Visible structures, even on the provided technology level.

HM Haustechnik Melsungen

For implementation of the ventilation technology, B. Braun relied on the local company HM Haustechnik Melsungen Service GmbH. A crucial factor in this decision was the fact that this partner had already successfully built and serviced the older ventilation system for PNS that had been used to date.

As a result, HM had a track record of the flexibility and commitment required in order to master the tight schedule of the construction project. During later maintenance of the system, the operator will also benefit from a regionally located, expert company that guarantees fast response times in case of a service call.

The interfaces between clean room construction, ventilation installation, and control and process technology are particularly significant challenges in such complex pharmaceutical projects. The company successfully built a clean room ventilation system for the production area with three clean room zones, in accordance with GMP, within the specified time period.

Tresolid

Clean rooms are characterized by cleanliness, openness and functionality. These properties are also reflected at PNS in the specially manufactured furniture in the production area. It was developed



and produced by the Tresolid company. B. Braun has collaborated with this company from Bad Wildungen for many years in the design and execution of clean room furnishings. Together, through constant modifications and innovative ideas, they have developed furniture systems for a wide range of clean room configurations

Collaboratively creating innovations

Tresolid develops and creates quality furnishings for clean rooms.



and application cases at B. Braun. This is a challenge, because in addition to having a functional design, the furniture must also withstand years of intensive contact with cleaning and disinfection agents and meet strict pharmaceutical GMP requirements. These requirements are best fully met with materials such as high pressure laminates with antibacterial coatings. Processing this material requires a high level of technical expertise and solutions that bring design and functionality together. B. Braun has relied on Tresolid's expertise repeatedly for many years.

Vitec

Glass walls create perspective, cleanliness and transparency – values that are given particularly high priority in the compound-ing production.

Together with the companies Vitec and Bayer-Bitrotechnik, B. Braun was able to create a clean room that achieves these goals, but also reflects aesthetics, design and transparency. The "heart" of the production facility in particular, the Class B production area, is intended to radiate openness and cleanliness through a maximum proportion of glass. The clear view ensures visual communication in production. For such transparency with simultaneously optimized airflow, a new approach to return air guidance was needed: Vitec and Bayer-Vitrotechnik developed self-supporting return air shafts made of glass.

The material passes that connect the production area to the adjacent spaces also received a new design that supports







High standards for elegant design, functionality and ergonomics are met to the smallest detail.

optimal product flow. These have to be especially wide and as fully transparent as possible, and must maintain the defined positive pressure. B. Braun and Vitec partnered to collabora-

Transparency and functionality

Vitec ensures a clear view and innovation in the clean room.



Clean room installation advancements, sophisticated to the smallest detail: active pass-throughs in the production area, refrigerated locks and self-supported, full-glass return air shafts.

tively develop a completely new prototype that meets these requirements.

The horizontal flow refrigeration lock is another innovation, developed and installed for the first time by B. Braun Engineering in collaboration with Vitec. The goal is to facilitate the process of outfeeding compounding products. The products should be transported as little as possible. The freshly manufactured bags, which require refrigerated storage, now go directly to a refrigerated area and can be removed the next day from the other side, without having to be transported another time. This new development simplifies the manufacturing process, guarantees that the refrigeration chain is complied with and improves handling for PNS employees.





Architecture

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