Whitepaper

Quality by Tradition

Sterile pumps for the pharmaceutical industry

GEA engineering for a better world

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Content

Page

Quality by Tradition – sterile pumps for the pharmaceutical industry

When selecting pumps, besides availability and easy maintenance, pharmaceutical manufacturers place cleanability at the top of the agenda. To succeed in global competition, the pharmaceutical industry and its contract manufacturers must produce as cost-effectively as possible – without losing sight of reliability and safety. For many years now, GEA has been committed to ensuring maximum process, material and failure safety. In combination with modern, energy-efficient, speed-controlled motors, the proven hygienic pumps of this global player open up wide-ranging improvement potential for pharmaceutical companies.

GEA Hilge is "the" competence center for hygienic pumps within the globally active GEA Group. The high-quality pumps "Engineered in Germany" ensure reliable processes for pumping demanding products in the pharmaceutical, biopharmaceutical and personal care industries.

Requirements for sterile pumps in the pharmaceutical industry

In the pharmaceutical industry, pumps and their requirements are subject to a wide range of international laws, regulations and guidelines. The maximum level of microbiological safety must be guaranteed for the entire production process. In this respect, the certified cleanability plays an important role. No less important are the reliable sterilization/sanitation and certification of the properties and origin of metallic and non-metallic materials. The documented surface roughness and ferrite content, as well as extensive welding documentation, can also be part of the standard scope when it comes to the qualification of a pump in a pharmaceutical plant.

Core requirements of operating companies in the pharmaceutical and biopharmaceutical industry: FDA- and GMP-compliant components, high system availability, low maintenance and servicing effort, and maximum cleanability. The focus is always on hygienic, reproducible production, especially for sterile pharmaceuticals. To achieve this, plant designers, equipment manufacturers and component suppliers must take into account a whole range of aspects, beginning with an elaborate production process and ending with machines/components in hygienic design,

Did you know…

…that in pharmaceutical production all of the legal regulations, rules and standards listed below must be observed?

- FDA CFR
- GMP Guideline (75/319EEC)
- ASME-BPE
- EHEDG
- EU Machinery Directive (2006/42EC)
- DIN EN 1672-2, Food Processing Machinery – Safety and Hygiene Requirements (Basic Concepts)
- DIN EN 12462 Biotechnology (Performance Criteria for Pumps)

including sophisticated cleaning processes. The more hygienically the plant is designed, the shorter the CIP and sanitation times.

Good cleanability

Plant cleaning is essential for process safety and a critical issue in manufacturing pharmaceutical products. The more consistently the Hygienic Design principles have been implemented, the safer the cleaning and the lower the effort involved (time, temperature, detergent concentration). Due to the high consumption of water and detergents, cleaning is also of great importance from an economic point of view. The amount of energy required for heating the detergents is considerable. And the longer the cleaning process takes, the higher the losses caused by production downtime.

If the equipment has been consistently designed in accordance with the Hygienic Design principles, the cleaning effort and time required are significantly reduced. As a result, the pump in the CIP circuit runs for a shorter period of time, and therefore consumes less energy. Ultimately, Doc. 17 „Hygienic Designs of Pumps“ is of decisive importance for the qualification of a sterile pump in pharmaceutical plants, according to the EHEDG guidelines.

The first pump of the HYGIA series from 1962

Did you know…

…that Philipp Berdelle-Hilge was a pioneer in the field of hygienic pumps? Even during the development of his flagship Hilge HYGIA more than 50 years ago, he attached great importance to good cleanability. He was the first to decide on a pore- and blowhole-free deep-drawn version of the ring housing, while many other manufacturers still use cast housings today.

The plant components installed directly in the production area, such as pipelines, pumps, valves, fittings, etc., must not contaminate circulating media (high-purity water, pure steam) or products (cell cultures, solutions from the fermenter) – neither by the penetration of undesirable substances

from outside, nor by the materials used. Both manufacturers and operating companies therefore prefer high-quality stainless steel, which ensures cleanliness, corrosion resistance and a long service life.

The standards applied to the purity and reproducible quality of raw materials, active ingredients and end products are high. The manufacturing processes must be validatable, but also efficient and resource-saving. Optimized plant concepts to improve productivity and plant safety are one of the decisive factors for high competitiveness. This can only be achieved on the basis of sophisticated components that interact safely and effectively.

No dead spaces, no surface defects

Hygienic Design for pumps means: easy cleaning of all parts in contact with the media to prevent organic and inorganic contamination. Equally important in the pharmaceutical industry is the selection of the right materials for a high-quality and safe process. The main criteria for pump cleanability are the absence of dead spaces and a gap-free design of all internal parts. This applies, inter alia, to the mounting space for the mechanical seal and the arrangement, attachment and dimensioning of the draining system for residual liquid.

Where dead spaces cannot be avoided, the aim is to reduce them to the minimum. If gaps are inevitable, a minimum width must be specified to ensure optimal accessibility for the cleaning media.

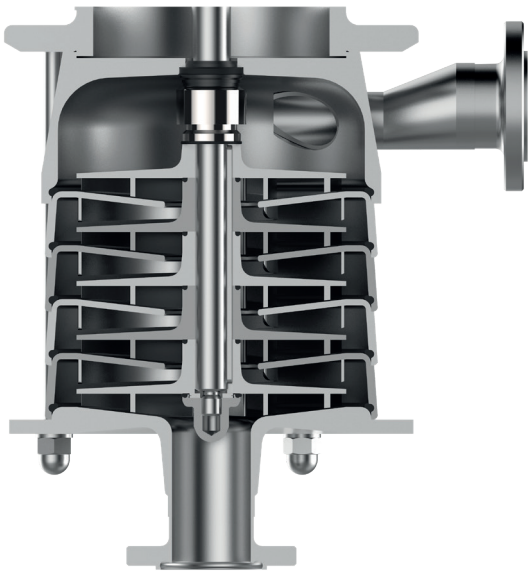
Did you know…

…that complete draining of residual liquid is essential? Ideally, no drain valves are required for this purpose (self-draining design). Even if the surfaces are inclined at an angle of only 3°, the liquid can run off completely, as in the vertical multistage pump series GEA Hilge CONTRA.

The wetted surfaces should be free of defects (cracks, scoring, scratches) and, in the case of cast stainless steel, void-free so as not to provide a habitat for microorganisms. Electropolished surfaces are therefore well suited. Electropolishing improves the corrosion resistance of the material, as well as its durability (no microcracks). The low adhesive properties of the surface facilitate cleaning.

To ensure safe sterile process conditions, non-porous rolled or forged low-carbon steel of grade 316L (1.4404 or 1.4435) is recommended (no stainless steel investment casting). Depending on the requirements, the pumps are offered according to different sterilization standards with surface roughness from Ra ≤ 0.8 µm to Ra ≤ 0.4 µm.

Conclusion: Electropolishing produces a very smooth corrosion-resistant surface. Cleanability is evaluated based on a validated cleaning procedure (defined initial state, procedure and final state).



Sectional view of the GEA Hilge CONTRA

Did you know…

…that it's not enough for the pump itself to be hygienic? The connections must also comply with the Hygienic Design principles. Incidentally, the same applies to the mechanical seal, drain system and O-rings. Only then can a hygienic pump be cleaned in accordance with the EHEDG regulations. All seals must be selected with regard to their durability, CIP/SIP capability and FDA conformity.

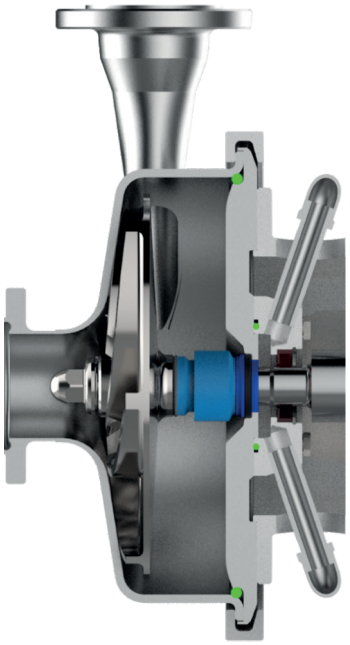
The critical importance of the seal

Special attention must be paid to the shaft seal of the pump, as it is the number one cause of failure.

Requirements for sterile mechanical seals:

- Enclosed and flushed sterile mechanical seal
- CIP/SIP compatible design
- Chemical resistance to product, cleaning agents and sterilant
- Preferred use of unflushed mechanical seals or mechanical seals with pressureless flushing
- If a flushed mechanical seal is essential for technical reasons, a sterile flushing medium must be used. This applies in particular when working with an increased sealing pressure.

Mechanical seals made of SiC/SiC composites and O-rings made of EPDM are the de-facto standard for pumping pharmaceutical water. Double-acting mechanical seals only in tandem design with pressureless flushing (lost flushing), in special cases a tandem seal for operation under super-imposed pressure.



Sectional view of the GEA Hilge HYGIA

Did you know…

…that a mechanical seal located in the product chamber provides significant advantages in the cleaning process?

The single-acting shaft seal is an internal mechanical seal, which is arranged in the pump chamber and freely flushed. This ensures CIP/SIP capability and effective lubrication and cooling of the mechanical seal.

Fluid-dependent design

The first step on the way to the ideal hygienic pump is the choice between centrifugal and positive displacement pumps – so it's good when a supplier like GEA offers both. The aim of each plant operator is to preserve the consistency, structure and ingredients of the product. In the pharmaceutical industry, the water typically transferred by pumps is of WFI (water for injection), PW (purified water) and AP (aqua purificata) quality. Other media to be transferred are infusion solutions, suspensions, nutrient solutions, alcoholic solutions, vaccines, blood plasma or ointments.

Centrifugal pumps dominate

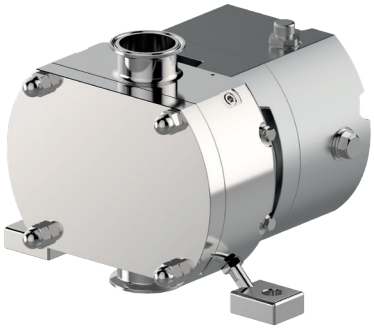
Centrifugal pumps are often the right choice, but not always. They are quite simple in construction and thus easy to maintain, and have a long service life if designed correctly. They can also be easily adapted to different operating parameters and are easy to clean in the Hygienic Design version. Due to the low investment costs, they are used in many process plants.

With viscous media, however, they quickly reach their limits. From an economic point of view, the use of centrifugal pumps is largely limited to Newtonian fluids up to a viscosity of approx. 500 mPas. Criteria for the gentle transfer of sensitive products include hydraulically optimized piping and cavitation-free operation. Speed control is always to be preferred to throttling the flow rate (see also the chapter about the advantages and disadvantages of frequency converters).

There is no question that centrifugal pumps are and will remain the workhorses of the process industry – the figures vary between a market share of 75 to 80 or even 90 percent. Only a narrow niche market remains for positive displacement pumps, the particularly „difficult cases“ so to speak. They are also at a disadvantage when it comes to price.

Positive displacement pumps as problem solvers

With increasing viscosity and higher solids contents, positive displacement pumps come into play. Their big advantage: They convey a set volume depending on the motor speed, but almost independent of the pressure. This is why they are suitable, for example, for processes in which a precise and gentle transfer is particularly important.



GEA Hilge NOVALOBE

GEA Hilge NOVATWIN

Arguments in favor of the gentle handling of sensitive products are, above all, the low pulsation level by means of multilobes in the case of rotary lobe pumps, and the near pulsation-free transfer by means of precision screws in the case of screw pumps. This makes the pumps ideal problem solvers for filling tasks, and approaches the accuracy of dosing pumps for mixing applications. Therefore, rotary positive displacement pumps clearly prevail over the oscillating versions of our competitors.

The pumps are mainly used for small or medium flow rates, but due to their function and design are also ideally suited for a wide range of viscosities and sizes of solids. Even with abrasive media, positive displacement pumps from GEA offer the perfect solution for a wide range of products.

In some cases, these pumps can also cope with additional cleaning tasks, so that several applications can be handled with a single pump, thus removing the need for not only the additional pump but also the complex multi-pump control scheme.

Did you know…

…that the GEA Hilge NOVALOBE rotary lobe pump and the GEA Hilge NOVATWIN twin screw pump handle even the most sensitive products, such as blood plasma, gently and with low pulsation and shear forces? Both can be completely emptied of residues and are fully CIP/SIP-capable, which shortens production downtimes and thus has a positive effect on the operating company's revenue.

Conclusion: GEA offers single and multistage centrifugal pumps for horizontal or vertical installation as per the requirements of the pharmaceutical, biopharmaceutical, beverage and food industries. The portfolio is supplemented by a rotary lobe pump and a twin screw pump series. Developed and manufactured in accordance with international standards and the Hygienic Design guidelines, all sterile pumps meet the requirements of operating companies with regard to the absence of gaps and dead spaces and the use of high-quality corrosion-resistant Cr-Ni-Mo steels with defined quality and surface roughness levels. In addition to product transfer, the pumps are also designed for use in CIP cleaning and SIP disinfection circuits. GEA pumps are supplied with comprehensive documentation to support the validation and FDA approval of pharmaceutical plants: Factory certificate/acceptance certificate according to 2.2 DIN EN 10204; material certificate according to 3.1 DIN EN 10204; FDA-USP Class VI certificate of conformity for the sealing and other materials used; surface roughness measurement report; ferrite content measurement report. All types are designed in accordance with the EHEDG guidelines.

Where frequency converters are worth considering

Realistic estimates (Motor Challenge Program; Hydraulic Institute) assume that between 20 and 25 percent of the electricity generated worldwide is consumed by pumps or their motors. A quarter of them are operated in process plants.

Even if older pumps work reliably, they are notorious for their low efficiency. On the one hand, this is due to the formerly common practice of oversizing any type of equipment; on the other, the hydraulic and drive-side efficiency of modern pump equipment has improved. Another issue is that plants change over time, whereas experience shows that pump equipment is usually not adapted accordingly.

Did you know...

…that the oversizing of pumps is still very common? And here's how it happens: Everyone involved in the ordering process adds "a little extra" to be on the safe side. Such safety margins, even if only 3% per person, can lead to a larger motor or, worse, a larger pump being purchased. But it is a deceptive safety. Cavitation increases during partial load operation, which in turn increases the probability of failure.

The search for new active ingredients requires creativity and a willingness to experiment. This does not, however, apply to pharmaceutical production. Product quality, plant availability and hygiene have top priority. The immense effort involved in the validation and documentation of a manufacturing process for an approved product also explains the reluctance of the operating companies. Strict regulations are usually the main reason why in the pharmaceutical industry optimization potential is exploited only hesitantly.

In order to ensure cost efficiency, plants must be operated as close as possible to their

optimum.. The be-all and end-all is a proper pump design (pump operating point close to the optimum, hydraulically correct dimensioning of the piping), energy-efficient motors, frequency converters (FCs) for speed control, efficiency-optimized hydraulic system and loss reduction in coils and bearings.

Centrifugal pumps are subject to the laws of affinity. This means (1) the flow rate is directly proportional to the speed, (2) the discharge head of the pump varies with the square of the change in speed, and (3) the power varies with the cube of the speed. So if the speed is reduced by 50 percent, power consumption is reduced by an impressive 87.5 percent. In short: The use of variable-speed drives is economically attractive when pressure and flow rate requirements vary greatly.

The power adjustment of the pumps via throttle valves or bypass circuits is suboptimal from an energy, hygiene and cleaning point of view. With fixed-speed pumps, the product to be transferred can be compromised by high shear forces resulting from higher speeds. Last but not least, more energy (i.e. heat) than required is transferred to the medium. This is always a disadvantage with regard to possible microbiological contamination. Nevertheless, FCs are not the solution for every problem. This is because they cause additional losses in the system, and should only be used if the motor is not operated at full speed. At constant process conditions, it is generally recommended to adjust the pump exactly to the required operating point (e.g. by trimming the impeller).

Arguments against the use of FCs...

- Higher investment costs
- Costs for EMC shielding and side effects, such as harmonics in the network. External filters always cause additional losses. Space and air-conditioning requirements for filters must be taken into account in control cabinets for external FCs.

...and in favor

- Precise and energy-saving adaptation to varying power requirements.
- Variable speeds are necessary or advantageous for the process.
- Commissioning effort and number of control valves and thus the total costs are reduced.
- Most gentle product handling.

Energy efficiency and technological advantages

Variable-speed pumps not only save energy, but offer many technological advantages. For example, in filtration processes, which are playing an increasingly important role in process technology. In membrane filtration processes, the product supplied is pumped across the membrane surface at high speed. Pumps provide the high volume flow required for this application, and are adjusted to the desired power levels by means of integrated frequency converters. This is necessary, inter alia, because the pressure difference of filter systems increases with increasing filtration time – an indicator of filter exhaustion.

If a constant flow rate is required, a flow meter provides the current actual value and the pump compensates for the decreasing flow rate by increasing the speed as the back pressure rises. Thus, it is also possible to compensate for varying conditions on the suction side of the pump, for example, for a different suction head after changing over to a different tank.

At the design stage, the power of the centrifugal pump is always selected on the basis of the maximum possible demand. Nevertheless, the pump is operated in the partial load range throughout almost the entire filtration process. Without a frequency converter, throttle valves or bypass circuits would have to be used for power adjustment. In this case, the fixed-speed pump would run at nominal speed and cause unnecessary stress on the transferred medium. Product variations or damage due to excessive mechanical stress would be virtually inevitable.

Speed control also scores points for product protection. It is a fact that circulation processes with throttled centrifugal pumps in ring lines and containers cause increased heat transfer to the pumped medium, which is almost always an undesirable side effect due to the possible thermal damage to and/or microbiological susceptibility of the product.

What are the greatest benefits?

The answer to this question is quite simple. Pharmaceutical companies can benefit above all during partial-load and weekend operation. To prevent contamination, plant operators keep their water distribution systems in motion 24/7. When using frequency converters, significantly less heat is transferred to the medium; as a result, less cooling is required, and energy costs are reduced. Moreover, the energy input may have a negative effect on product quality. The investment costs can also increase due to the additional heat transfer surface required.

The design of the pump is always based on the maximum demand for treated water and the minimum return flow. In practice, this means that conventional centrifugal pumps are oversized for many tasks – especially when partial quantities are required or for mere circulation on weekends. The customer's requirement for plant expandability, or the step-by-step commissioning of plant components in the case of new installations, also cause partial-load operation, which can cost the operator company dearly.

Integration or control cabinet?

Once the operating company has decided on a frequency converter, the next question is where to install it? There are two basic options: The external solution, i.e. installation in a more or less remotely sited control cabinet, or integrated FCs installed on the pump drive.

The primary selection criterion is, of course, power: With a maximum of 22 kW, integrated frequency converters cover a lower power range than versions designed for control cabinet installation, and are not suitable for every application.

For its hygiene pumps, GEA offers a high-efficiency motor with an integrated micro frequency converter and a PI (proportional-integral) controller with specific pump functions for a power range of 1.5–22 kW. It is suitable for most transfer tasks in the pharmaceutical industry.
The combination of motor with integrated frequency converter clearly exceeds the requirements of the energy efficiency class Super Premium Efficiency IE4 (IEC TS 60034-31 Ed.1).

Vertical GEA Hilge CONTRA with integrated frequency converter

Advantages of integrated drives:

- Complete system integration
- Simple and space-saving installation
- Robust design
- Lower cabling costs
- High dust and water protection
- Well-matched components
- Pre-configured and ready for connection on request
- Documented pump performance and functionality
- Smooth integration into higher-level control systems

An electronically controlled pump drive enables infinitely variable speed and power adjustment and the exchange of parameters and process data for central monitoring, control and possible visualization/recording. The keyword is traceability. In addition, frequency converters minimize the negative effect on sensitive media and reduce wear and energy costs. Regular maintenance of wearing parts reduces susceptibility to faults. As a result, the service life is increased. For CIP cleaning, a higher flow rate can be provided.

Sometimes it is necessary to decide between a large and small pump size. In individual cases, it may make sense to select the smaller pump with a larger motor and a frequency converter. In high-frequency mode up to 60 Hz, the higher performance required for, say, CIP operation is achieved, whereas in the more frequent standard operation mode up to 50 Hz, the small pump provides significantly better efficiency.
The additional costs of the frequency converter are partly balanced by the lower price of the smaller pump model. The fact that the pump, motor, frequency converter, software and controller all come from a single source ensures well-coordinated and, above all, reliable and safe interaction. Incidentally, the replacement of fixed-speed standard pumps of the same design causes no additional costs, apart from the frequency converter – the new pump only needs to be connected to the power supply and integrated into the piping.

Conclusion: Today, frequency converters are an integral part of sterile pumps. Continuous control via a micro frequency converter integrated in the motor is state-of-the-art. As a decentralized solution, this drive concept is an inexpensive, convenient alternative to external frequency converters, optimized for pump applications.

Sterile pumps from GEA Hilge

A wide portfolio of centrifugal and positive displacement pumps and decades of experience deliver the ideal pump for every application. Sterile pumps from GEA are characterized by reliability and efficiency, and ensure resource-conserving processes.

The pumps made of stainless steel and other high-quality materials meet the highest hygiene standards, are easy to maintain and offer good cleanability. Their robustness promises a long service life and high reliability.

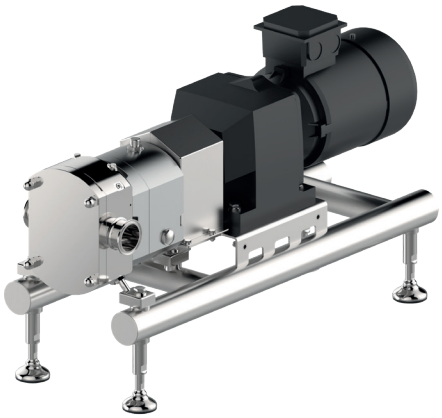
At GEA, service is a top priority. A worldwide service network and qualified specialists for professional in-house repairs, as well as global spare parts logistics guarantee fast support in case of emergency.

GEA Hilge HYGIA

The „Swiss knife“ of hygiene pumps: top quality, reliability and flexibility. The wetted parts meet the requirements of the 3-A, QHD and EHEDG standards. The pump is equipped with a fully enclosed mechanical seal with a unique sealing surface design, and is also available in a high pressure version.

GEA Hilge CONTRA

Available as single and multistage centrifugal pumps. The pumps ensure extremely reliable operation under the toughest operating conditions. The consistently hygienic and aseptic design and the use of non-porous materials combine to create perfect solutions for many applications in sterile and hygienic processes, especially WFI loops.

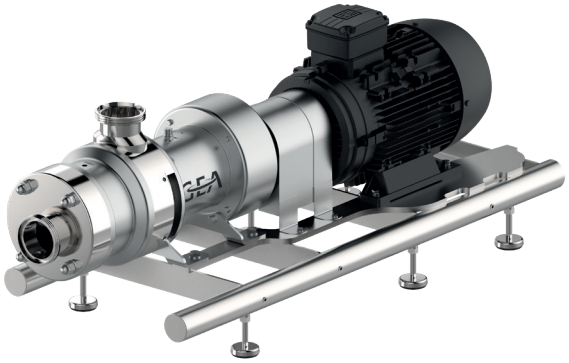


GEA Hilge NOVALOBE

This rotary lobe pump was developed especially for highly viscous media and for applications requiring gentle transfer. With its vertical connections, the pump is completely drainable and meets the EHEDG requirements. It is available with a double-sealed, aseptic front cover, which provides better protection against the penetration of bacteria.

GEA Hilge NOVATWIN

This flexible twin screw pump enables production and CIP processes with a single pump. It meets the highest hygiene requirements, ensures reliable production and, thanks to the pump design, guarantees gentle product handling with almost no pulsation.



GEA Hilge SIPLA-HT

This single-stage self-priming side channel pump is particularly suitable for SIP/CIP return systems and applications with high gas content. The hygienic and robust pump is made of pore-free and blowhole-free Cr-Ni-Mo steel. The reversible flow direction facilitates emptying and refilling processes.

Glossary

ASME-BPE

American Society of Mechanical Engineers: Bioprocessing Equipment

International standard for the design and construction of biopharmaceutical production plants

CIP/SIP

Cleaning in Place/Sterilization in Place

EHEDG

European Hygienic Engineering and Design Group

EPDM

Ethylen-Propylen-Dien-Kautschuk

FDA CFR

Food and Drug Administration Code of Federal Regulations

Body of regulations for the Federal law of the United States. The GMP regulations for pharmaceutical products are stipulated in the Code of Federal Regulations 21 CFR Part 210/211.

FC

Frequency converter

GMP

Good Manufacturing Practice

This directive lays down principles and guidelines of good manufacturing practice for medicinal products for human use. It represents a comprehensive quality assurance system for the manufacturing of certain products in order to achieve maximum consumer protection..

SiC

Silicon carbide

engineering for
a better world

We live our values.

Excellence • Passion • Integrity • Responsibility • GEA-versity

GEA is one of the largest technology suppliers for food processing and a wide range of other industries. The global group specializes in machinery, plants, as well as process technology and components. GEA provides sustainable solutions for sophisticated production processes in diverse end-user markets and offers a comprehensive service portfolio.

The company is listed on the German MDAX (G1A, WKN 660 200), the STOXX® Europe 600 Index and selected MSCI Global Sustainability Indexes.

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