World-Class Pharmaceutical Processing Solutions

A complete range of specialist solid and liquid dose technologies
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GEA, a global specialist in solid and liquid dose technology

Combining trusted technology with an ongoing program of innovation and price/performance leadership, GEA provides process solutions for the pharmaceutical, biopharmaceutical, biotechnology and nutraceutical industries.

With a long history of expertise and an unparalleled depth of know-how in the pharmaceutical and greater life science industries, our portfolio includes single units, modular systems and complete production lines for powder processing, oral solid dosage forms, parenterals, sterile liquids and semi-solids.

Our activities include partnering with customers to develop new products and enhance clinical effectiveness, the supply of R&D-scale and standalone production-scale equipment, and the installation of completely integrated process lines.

Our many years of experience and successful installations around the world have provided us with a deep and fundamental understanding of a variety of mission-critical processes, such as batch and continuous granulation, drying, pelletizing and coating, contained materials handling, tablet compression, freeze drying, fermentation and liquid formulation, separation, homogenization and cell disruption, to name a few.

With a portfolio that’s “Packed with Inspiration,” GEA has built a reputation for matching creativity with technology, but it’s our wealth of experience and knowing how to bring these technologies together in a creative way to meet your needs that really matters.

Working closely with you, the customer, to develop new products, reduce time-to-market and enhance clinical effectiveness, we provide a wide range of services, including test facilities, technical excellence, process evaluation and product development to award-winning technology, project management and ongoing support.

GEA is your single-source supplier of robust, flexible and cost-effective manufacturing solutions that maximize operational reliability and productivity. We offer the largest variety of process technologies and boast an unrivalled history of identifying the most appropriate solution for your specific application.

From Alaska to Australasia and from MUPS to mAbs, GEA is the only supplier capable of meeting your specific liquid and powder processing requirements, saving you from searching the world for specialized machinery. No other company serves as many industries in as many countries as GEA!
**SOLIDS:** Powder Handling, Granulating, Drying, Compression & Coating

Whether batch-based or continuous, for contained production and/or direct compression applications, we have the know-how, equipment and expertise to optimize your oral solid dosage production.

Innovation is at the heart of all our products; it’s what makes them different. The quest for continuous innovation is the force that drives us every day, and flexibility, performance, accuracy and control are the criteria that focus our thinking. Everything we do is aimed at improving these key factors to help you to make better products and improve productivity.

GEA supplies standalone machinery, engineering services and completely integrated process lines for even the most challenging products, including

- potent APIs
- MUPS tablets
- effervescents
- multilayer pellets.

Plus, as containment experts, we offer the largest selection of solutions for contained processing based on a thorough risk analysis. Our technology is world renowned for its reliability, flexibility and economy. We offer truly rapid changeover solutions, increased productivity, flexibility and safety.

However, it’s much more than that; it’s about how we work with you, the customer. We understand your needs; we use our expertise and know-how to develop solutions and optimize processes that bring your products to market quickly and provide the commercial advantage you need.

**AWARD WINNING CONTINUOUS PLATFORM**

It’s thanks to GEA’s ConsiGma™ technology that, in 2015, Vertex Pharmaceuticals became the first pharmaceutical company to receive FDA approval for a therapeutic that was both developed and commercially manufactured using a continuous manufacturing platform.

And GEA’s miniaturized, mobile ConsiGma™ 25 unit forms the basis of a groundbreaking, award-winning collaboration with Pfizer and G-CON to develop the next generation of Portable, Continuous, Miniature and Modular (PCMM) solutions for pharmaceutical production.

Furthermore, in 2016, Pfizer proudly received the ISPE Facility of the Year Award (FOYA) for Equipment Innovation for the project “The Portable Continuous Miniature and Modular (PCMM) Collaboration.” Commenting on the award, Frans K.A. Maas, Vice President Pharma Solids, said: “We’re convinced that this platform, based on GEA’s ConsiGma™ continuous manufacturing technology, provides significant benefits to both the generic and the ethical industry segments when compared with more traditional batch technologies.”
PAT-ENABLED CONTINUOUS TABLET PRODUCTION

GEA and Siemens have joined forces to advance continuous production processes in the pharmaceutical industry. Bart Moors, Director, Global Account and Project Development, Life Sciences, Siemens, explains: “Together with several major customers including Merck and GlaxoSmithKline (GSK), Siemens launched a PAT initiative back in 2007 to focus on non-continuous processes. Two years later, in the context of this collaboration, GSK posed the question: “Is it possible to run a batch-based system as a continuous process?” Subsequently, a joint initiative with GEA was founded to bring an integrated continuous tablet manufacturing line to the pharmaceutical and life science industries and establish proof-of-concept.

“Historically,” adds Frans K.A. Maas, Vice President Pharma Solids, GEA, “the pharmaceutical industry gathered process data from single samples and that information was recorded and stored as a paper-based hard copy. But, when the development and implementation of automated systems began to gather speed in the mid-nineties, managing the vast amount of data that was generated became untenable. We had to ask ourselves: what do we do with all the data and how can we both reduce risk and improve quality?”

For more than 20 years, the batch-based production of blockbuster solid dosage forms dominated the industry. Profitability was such that companies were not incentivized to innovate or risk developing new manufacturing technology. However, in the post-blockbuster era, it is increasingly recognized that material costs during drug development are significant, making time-to-market even more critical, new drug products are likely to be manufactured in much smaller quantities and that, for novel treatments, the development of a commercial manufacturing process is not guaranteed.

A single continuous manufacturing (CM) line can be used to process any volume of product, from small quantities for formulation development and design of experiments (DoE), through to clinical trials and the full-scale manufacture of new chemical entities and high volume generics without the need to invest in costly new equipment or dedicated plant. Product output is rapid, scalable and can be adjusted according to need, such as in the event of major disease outbreaks.

The biggest driver is, of course, cost, along with faster throughput, less active pharmaceutical ingredient (API) is required in development and scale-up, the reduced need for good manufacturing practice (GMP) space, less out-of-specification material, flexibility, etc. There is, however, some uncertainty about registration.

“We’ve already received a great deal of very positive feedback from the industry,” adds Frans: “Smaller companies in particular seem to appreciate that the combined experience of GEA and Siemens makes it much safer (less risky) and easier for them to move into continuous processing. We’re also seeing considerable interest from contract manufacturing organizations.

The non-exclusive collaboration will deliver both production benefits, in terms of reduced project execution risk, higher quality and cost-effective manufacturing, and customer benefits in the form of seamlessly integrated technologies, expertise and support.

In recent years, regulatory pressure and changing approaches to drug development have spurred the pharmaceutical industry to look beyond its batch processing history. Now, Siemens and GEA have taken a major step forward on the path to making continuous manufacturing mainstream.
From powder to coated tablet and from R&D to full-scale manufacturing, no other supplier offers such a comprehensive range of batch-based technologies for oral solid dosage form production.

Whatever your application, no matter how challenging, GEA’s contained powder handling, granulating, drying, compression and coating solutions will meet and exceed your individual requirements.

Designed with integration in mind, you can select from a variety of standard process modules to suit your project needs.

Granulation

In the pharmaceutical industry, tablets remain the most commonly produced oral dosage form; most fine pharmaceutical compounds require granulation to improve their flowability and processing properties before tableting. As such, granulation, which allows primary powder particles to adhere and form granules, is one of the most important unit operations in drug manufacturing.

A number of different granulation and compression technologies are available to pharmaceutical manufacturers, all of which have individual strengths and weaknesses depending on the specific application. However, the theory of granulation is often poorly understood, and the selection of a particular machine and granulation method is frequently made on the basis of tradition and the operator’s experience, rather than by using strict scientific or cost-benefit criteria.

Whatever your application or requirement, every granulation and drying plant from GEA is a unique union of proven technology and individual solutions. Based on standard components, we supply plants for cGMP production that are configured to meet the customer’s specific requirements.
Successful Tableting
As a single-source supplier of state-of-the-art tableting technologies, our innovations include a unique dual control, PAT-compatible technology that monitors and controls tablet weight, hardness and density with an accuracy that cannot be achieved any other way.

Weight is controlled at pre-compression and hardness is controlled at main compression. As a result, weight and hardness can be controlled simultaneously and continuously on a standard tablet press.

GEA also offers adjustable dwell times at pre-compression (by up to 300%) without slowing the press: this functionality allows an increase in dwell time at pre-compression that’s independent of machine speed, resulting in higher outputs and more consistent tablet quality.

In addition, constant dwell times with adjustable compression speeds can be used to match the production capacity of the line without influencing tablet quality. Other unique features ensure a constant flow and equal distribution of powder that are without equal, as well as integrated data collection and analysis, and advanced process control.

Materials Handling
GEA is a trusted supplier of material handling equipment with significant expertise in containment and the provision of integrated solutions to the global pharmaceutical and healthcare industries. Taking an individual approach to each customer’s needs, and applying our extensive experience and know-how, we combine performance excellence with technological innovation to deliver long-term competitive advantages.

With thousands of installations worldwide, GEA has developed an outstanding reputation for quality and service to become the clear leader in contained materials handling technology, including powder handling, intermediate bulk container (IBC) systems, containment valves, container systems, in-container blending, tablet handling and IBC washing.

Our distinctive specialization lies in the integration of BUCK® containment technology into complete solutions for pharmaceutical solid dosage form facilities.
The last 20 years have seen a significant increase in the need for contained handling and processing in the pharmaceutical industry, driven by the development of more potent APIs and a stronger focus on health and safety by the regulatory authorities. Containment issues have become a vitally important aspect of solid dosage form production. Active pharmaceutical ingredients (APIs) are becoming increasingly effective, with more than 50% of all new chemical entities (NCEs) being classified as potent (OEL <10 μg/m³); at the same time, the health and protection of operators, all over the world, is being put under an ever more intense spotlight.

Containment is the separation of the product from the people — and from the environment — by a barrier. Containment is used to prevent any negative impacts (contamination) being transferred from one area to another, and vice versa. Why is the pharmaceutical industry interested in containment? For two reasons: operator exposure and the prevention or elimination of cross-contamination. But how much containment is required?

“**A key point,**” says David Johnson, Sales Manager, Containment Technology, GEA, “**is that the required level of equipment and containment performance is not simply a matter of measuring the Occupational Exposure Limit (OEL) of the product. This is a common misconception and, as a result, there is a tendency within the industry to over specify.**”

He explains: “**Selecting an overly complicated solution means that the system is more difficult to operate, difficult to clean and maintain and, of course, more expensive to buy. It can be problematic to show that a particular solution is ‘good enough,’ but it can be done. By understanding containment and looking at the product, the operator and the equipment, we can create well engineered and better value solutions.**”

**How Much Containment?**

In an ideal world, operators would not be exposed to a single molecule of a harmful substance; but, in the real world, this is simply not possible. Three main factors dictate how much containment is required and, therefore, which method of containment is best: the nature, especially the potency, of the API handled is of paramount importance; the type of process to be executed; and, lastly, the working regime of the operators.

The ADE (Acceptable Daily Exposure) describes the absolute amount of a specific drug substance that an operator can absorb without any negative health effects. The OEL defines the maximum concentration of a drug substance that can be tolerated in the air of the production room without imparting any negative effect on the health of the operators. Dust inhalation is recognized as the biggest risk to operator health and safety.
For visibly contained product transfer and the safe handling of potent products, the disposable Hicoflex® system is quick and easy to install and use.

In Summary
Containment is determined by the characteristics of the product, equipment performance and operator function. Operator exposure depends on the type of equipment being used, product dilution levels and frequency of operation.

As exposure can’t be fully prevented, the employer must ensure that the operator’s RDI of a hazardous substance doesn’t exceed the product-specific ADE by using suitable equipment. The company should only implement additional personal preventive measures when this cannot be guaranteed by appropriate technical options, including:

• eliminating the source of risk
• substituting the hazardous material with a less harmful one
• modifying the process
• using engineering controls to reduce exposure (contained handling)
• improving administrative procedures (SOPs).

The selection, placement and implementation of suitable containment equipment can be a daunting task; it requires an in-depth understanding of the overall process, primarily to ensure that the chosen equipment performs at the necessary level, but also, from a financial point of view, to prevent any expensive and unnecessary investment into an over-performing solution.

GEA not only offers the largest variety of robust and compliant hardware solutions for contained materials handling, but it also boasts unrivaled expertise in identifying the most appropriate solution and a thorough understanding of containment risk analysis.

GEA can assist and advise you to determine what level of containment is required where and when, optimizing the manufacturing process and making it efficient, safe and cost-effective.

We provide tailor made containment for the pharmaceutical industry – for now, and for the future.
The pharmaceutical industry is looking at continuous processing to improve production quality in an efficient and cost-effective way, and to comply with the increasingly stringent manufacturing acceptance criteria being put in place by the regulatory authorities.

Process intensification in the pharmaceutical industry has led to the development of smaller and more compact equipment. With the goal of achieving more consistent process control and, ultimately, higher quality end products, manufacturers are increasingly moving away from batch-based systems and switching to continuous manufacturing (CM).

Providing increased yields, lower utility consumption and reduced waste, CM presents a paradigm shift in drug production and meets the industry’s demands for faster product development, reduced costs, improved production economics and increased manufacturing flexibility.

Dramatically reducing development time and costs, and eliminating scale-up, the benefits of continuous manufacturing are manifold. Real-time quality assurance is enabled by the application of inline PAT systems that continually monitor processing conditions and product quality. This facilitates real-time product release against a backdrop of less invasive regulatory oversight, as well as the reduced use of resources and energy, lower product losses and minimized downtime.

The ability to run CM plants for extended periods also decreases product wastage associated with each plant start-up and shutdown, while the high degree of automation minimizes the need for manual intervention.

When the US Food and Drug Administration (FDA) advised the pharmaceutical industry to get ready for the concept of continuous drug production, GEA was already there. We’ve been running a continuous line since 2007! With decades of experience in pharmaceutical processing technologies and engineering, GEA has invested a significant amount of time and energy into the development of advanced CM technologies and pioneered the world’s first continuous wet granulation line to produce OSD formulations.

SOLIDS: Continuous Processing
The implementation of CM enables a more efficient way of making drugs in a fully integrated and closely controlled process that gives excellent product consistency. The highly versatile ConsiGma™ manufacturing platform, for example, combines multiple technologies that convert powdered raw materials into coated finished drug products in one single, closed unit.

The platforms take up 70% less space than batch plants, so can be built more quickly and with much lower capital expenditure. Individual ConsiGma™ units can be designed, deployed and approved for commercial-scale manufacture within a year, compared with 2–3 years for traditional plants. Furthermore, whereas some batch-based operations take weeks to produce tablets, the same products can be manufactured within minutes with a continuous system.

The ability to establish smaller, cost-effective and resource-efficient plants increases the chance that local manufacturing sites can be established to meet regional needs and so reduce global transport requirements. GEA now has more than 47 full continuous OSD manufacturing installations operational worldwide.

**Flexible and Scalable**

A single continuous manufacturing line can be used to process any volume of product, from small quantities for formulation development and design of experiments (DoE), through to clinical trials and the full-scale manufacture of new chemical entities and high volume generics without the need for investment in costly new equipment or dedicated plant. Product output is rapid, scalable and can be adjusted according to need, such as in the event of major disease outbreaks.

**Conclusion**

GEA believes that the development of small-scale, CM systems will be one of the most significant changes in the pharmaceutical industry in the next 10 years. Flexible development options will facilitate the commercial manufacturing process and enable greater process understanding to be achieved with smaller quantities of material.

As a trusted innovator of manufacturing concepts, analytical technologies and processing equipment, GEA has the capability and will continue to play a major role in the global drive to develop continuous OSD manufacturing solutions that improve the quality, efficiency and cost-effectiveness of pharmaceutical production for the ultimate benefit of patient health.
With a total footprint of 1100 m², including 200 m² of technical space, the GPSC epitomizes the state-of-the-art in oral solid dosage (OSD) form testing, development and optimization, and offers a full range of batch and continuous manufacturing technologies.

From cost assurance and process enhancement to real-life simulations and test and loan machines, we provide a unique range of services that are designed to improve production and expedite time-to-market.

The GPSC offers
- customer demonstrations and trials on our batch and continuous equipment
- training sessions and classes
- hands-on laboratory experience
- pharmaceutical product development assistance
- CQA evaluation support
- testing of new concepts (equipment and advanced controls)
- scale-up from laboratory to production (1:10)
- process development/refinement to increase the understanding and capability of GEA equipment.

A trusted supplier of plant and equipment, GEA offers manufacturers all over the world the opportunity to enter into a profitable partnership to develop products, processes and technologies.

The company combines advanced in-house technology with a thorough understanding of the processing industries to help customers maximize their development results, gain more know-how and discover additional opportunities for their applications.

GEA’s centers of excellence provide access to a full range of test facilities and teams of experts, all of whom work closely with their customers to optimize procedures and evaluate their products, enabling them to achieve their process and production goals.

A PORTFOLIO OF INNOVATION
GEA offers such a comprehensive assortment of tableting technologies, from powder handling to granulating, pelletizing, drying, compression and coating, including the first ever continuous high shear granulation, drying and tableting system, which is set to revolutionize OSD processing.
Batch Processing Technologies
The GPSC enables you to investigate all the batch-based solid dosage production techniques offered by GEA, in lab-, pilot- or production scale.
• IBC blending
• High Shear Granulation
• Fluid Bed FlexStream™ Granulation
• Fluid Bed Top Spray Granulation
• Single Pot Processing
• Fluid Bed FlexStream™ Drying
• Fluid Bed FlexStream™ Coating
• Fluid Bed Precision Coating™
• Extrusion/Spheronization
• Tablet Compression
• Milling/Calibration

Continuous Processing Technologies
The GPSC enables you to investigate the possibilities that continuous manufacturing can offer for your production. In the GPSC, the following technologies are available for testing.
• Continuous Tableting Line CTL™ 25
• Continuous Direct Compression line CDC™ 50
• Off-line Continuous Feeder CF
• ConsiGma™ 1
• ConsiGma™ Coater

Worldwide Support
From solid dosage applications in the Wommelgem GPSC to the largest and most advanced spray drying facility in the world in Copenhagen, Denmark, and separation technologies in Oelde, Germany, we can help you to build quality into your processes, adjust key parameters to drive your critical quality attributes to the required target levels and bring new products to market in a quick and efficient way.

To discover more or organize a test, demonstration or training session, contact our dedicated, passionate and experienced team. With a long history of solid dosage form expertise, including more than 125 formulations, everyone at the GPSC is committed to going the extra mile to meet customer expectations. Wherever you are in the world, whatever your application, we’ll take you further, faster.
At a Glance: SOLIDS Solutions

Applications

- Formulation Development
- Anti-Cancer Treatments
- Antibiotics & Anti-Infectives
- Effervescents
- High Volume Production
- Highly Potent APIs
- Hormones
- Inhalable Fine Powders
- MUPS
- Pellets
- Tablets

Core Technologies

- **Granulation**
  - Addition of Liquid & Ingredients
  - Continuous Blending (NEW)
  - Continuous Granulation
  - Dry Powder Blending
  - Fluid Bed Granulation
  - Fluidized Spray Drying
  - High Shear Mixing
  - High Shear Granulation
  - Integrated Granulation
  - Liquid Mixing & Blending
  - Melt Granulation

- **Drying & Particle Processing**
  - Dispensing & Dosing
  - Dry Bonding
  - Extrusion
  - Fluid Bed Drying
  - Layering
  - Melt Pelletizing
  - Microwave Drying
  - Particle Pellet Coating
  - Pelletizing
  - Single Pot Processing
  - Spheronization
  - Spray Drying
  - Vacuum Drying
  - Wet Pelletizing

- **Tablet Compression**
  - Contained Tableting
  - Continuous Coating
  - Continuous Direct Compression
  - Continuous Tableting
  - Industrial Compression
  - Tablet Coating
  - Tablet Compression

- **Product Handling**
  - Contained Materials Handling
  - Dispensing & Dosing
  - Dispensing & Weighing
  - Handling of Bulk Ingredients
  - Mixing & Blending
  - Tablet Handling
Integration experts

- Analytics, Monitoring & Process Control
- Process Integration
- Cleaning & Sterilization
- CIP/SIP Technology

Utilities

- Air Conditioning & Chilling
- Cooling & Refrigeration
LIQUIDS: Sterile Process Solutions for Pharma & Biotech Industries

Drug production and the manufacture of active pharmaceutical ingredients (APIs) demands the very highest product quality and purity standards, as well as validated manufacturing processes.

As a supplier of sterile process plant with many years of experience, GEA can draw upon the comprehensive theoretical knowledge and expertise of its engineers to provide modern, bespoke and cost-effective process technology to manufacture new medicines according to cGMP guidelines and US FDA, SFDA and EMA requirements.

The process lines provided by GEA have a proven track record in API production, including fermentation, clarification, membrane filtration and separation, homogenization and micronization, crystallization, concentration, lyophilization and fractionation.

As well as complete integration with upstream and downstream processes, our standalone machines or package units guarantee a high yield of valuable substances and operate trouble-free, efficiently, reliably and economically throughout a long service life.

Based on established standards, our project teams will devise project documentation that’s specific to your individual requirements and competently deliver the project on time, on budget and to the agreed level of quality.

Offering a comprehensive range of services and project management, we guarantee successful outcomes and a tailor-made solution for your application.
Experts in aseptic process management, closed product handling, compliance with GMP requirements, gentle product treatment, the efficient recovery of active ingredients and reliable scale-up, we supply modules, components and complete lines for the production and purification of biotechnologically manufactured products such as vaccines, hormones and other therapeutic agents.

Equipment Specialists
GEA’s technologies include fermentation, mechanical separation, high-pressure homogenization and cell rupture, freeze drying, aseptic spray drying, plant control systems (SCADA and MES) and more.

Our product portfolio also includes a range of batch and continuous mixing, blending and formulation systems, including standard and custom-designed solutions for media preparation and formulation, as well as automation, data collection and CIP/SIP solutions.

From the planning phase to the construction and automation of turnkey plants and process lines that conform to stringent hygienic and regulatory requirements, GEA is dedicated to developing and supplying customer-orientated solutions.

As a competent manufacturer of complete process lines for the life science industries, GEA is a full-service provider of solutions that meet your exact requirements and specifications. From planning, development and installation to qualification and maintenance, our experienced engineers will collaborate with your project team to supply innovative and efficient process solutions for your applications.

Bioreactors, Fermenters and Vessels
GEA designs and manufactures a wide range of preparation and pressure vessels, fermenters and bioreactors that meet the needs of any microbial or cell fermentation process.

Preparation and pressure vessels from GEA set new performance standards and ensure that our customers’ central process components have competitive advantages. The surfaces of our preparation and pressure vessels are ground, polished and, if required, electropolished. All welds are smoothed to current GMP/FDA standards and exclude even the smallest cleaning dead spaces.

Examples include preparation vessels for the production of sterile products, buffer preparation vessels for blood plasma fractionation and media preparation vessels for pharmaceutical fermentation processes.
Our systems feature sterile design and high quality components, complemented by a fully automated control system and a full cGMP documentation package (optional), as well as equipment for temperature control, agitation, aeration, de-aeration and dosing.

Separators
Pharmaceutical biotechnology requirements are high, including aseptic process management, optimum cleaning capability, closed product handling, gentle product treatment, the efficient recovery of active ingredients and reliable scale-up. With separators designed specifically for this sector, GEA stands for reliable compliance with these requirements.

Homogenizers
Cell disruption: GEA homogenizers are fitted with specifically designed high efficiency valves for optimized cell disruption at the lowest possible pressure. Designed to comply with FDA and cGMP guidelines, they come with a full documentation package, including materials certification and traceability, FAT/SAT procedures and IQ/OQ support.

Micronization involves reducing the particle size of liquid pharmaceutical products using dynamic high-pressure homogenization to make a dispersion of active ingredients more stable for enhanced clinical effectiveness. Optimized particle micronization and homogenous distribution means that API bioavailability and drug tolerance is improved.

Flow Components
Our scope of supply includes raw material handling, mixing and blending, storage, end-of-line packaging, product recovery, cleaning and sterilizing in place, and automation. And, from basic engineering, through detail engineering and design, construction, installation and commissioning, we can provide a comprehensive range of advanced processing components that can be readily combined with our standardized modules (which form the basis of our proven systems).

Pumps: GEA offers a range of pumps, including centrifugal, self-priming and rotary piston versions. The technology has been designed specifically to keep flow paths free from dead corners, convey product evenly and gently, ensure high product quality, and use the minimum of energy, water and raw materials.

Valves: Core components in all piped process plants, GEA’s range of valves has an enviable reputation for reliability, efficiency, easy maintenance and low lifecycle cost. By using its experience, process knowledge and group know-how to integrate these best of breed technologies at the design stage or as retrofit components, GEA is able to build and maintain world-beating plants for its customers.

Inline Process Connections: Offering a variety of dead-leg free process components, matrix piping that converts plant equipment into closed systems, control instruments and sensors to maintain production process transparency, CIP/SIP systems and GEA’s VARINLINE® inline control and measurement technology, we can provide a comprehensive range of advanced processing components that can be readily combined with our standardized processing modules.

Tank Safety Systems: The safe, hygienic and effective cleaning of process tanks, and protecting them from excessive pressure and/or vacuum, is of paramount importance in the pharmaceutical industry. GEA offers a modular solution, based on standardized components, that ensures optimum plant availability and product quality, and reproducible cleaning. The VARITOP® Tank Safety System can be configured to match specific process parameters, cleaning methods and CIP/gas management requirements to ensure the safety and hygiene of process tanks of any size and shape.
**Expansion Compensators:** In large, rigid-piped valve matrices, uncontrolled heat expansion can cause pipes and valve housings to deform and impair the production process. Especially suitable for valve matrices and fixed process pipe systems, GEA’s VARICOMP® Expansion Compensators can be used to overcome thermal stress and prevent downtime. VARICOMP® benefits from a compact and pocket-free design, is CIP/SIP-compatible and is ideally suited to hygienic and aseptic process operations.

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**PandaPLUS 2000 Homogenizer**

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**HANMI PHARMACEUTICAL INVESTS IN GEA TECHNOLOGY**

GEA has been chosen by Hanmi Pharmaceutical, one of the largest drug manufacturers in Korea, to supply manufacturing equipment for a new plant that’s currently under construction in the city of Pyeongtaek-si in the Gyeonggi province of South Korea.

GEA will provide two production lines for insulin, including centrifugal separators, fermenters, flow components, homogenizers and a significant number of valves. The multimillion Euro order is scheduled for completion during 2017 and further reinforces the co-operative business relationship between the two companies.

The order from Hanmi includes equipment for two identical fermentation and media preparation lines, fully equipped with GEA VESTA® valves, for the production of a fragment of human immunoglobulin type G.

GEA is currently negotiating further equipment orders with Hanmi Pharmaceutical, which also include a large number of VESTA® valves. Being the largest order for aseptic pharma equipment in GEA’s history, the deal represents a breakthrough for the company in terms of supplying superior valve technology to the biopharmaceutical sector.
With access to some of the world’s most advanced manufacturing equipment and a wealth of expertise and experience to call on, GEA fundamentally understands the processes involved in vaccine production, the capabilities of the technologies employed and the engineering required to ensure that they operate at optimum capacity with the lowest maintenance.

With its unique blend of expertise and experience, GEA supplies standalone machines or package units that guarantee a high yield of valuable substances and operate efficiently, reliably and economically. Whether large or small, GEA can add value to any vaccine production project.

All vaccines, whether live (bacteria or viruses), inactivated (bacteria and viruses), toxoids or antigens, are produced using fermentation technology in fermenters, bioreactors or, in some examples, even hens’ eggs.

GEA is a market-leading supplier of complete fermentation systems for bacteria, yeast, mammalian cells and viruses, including:

- anaerobic tetanus fermenters with vibrating stirring systems (up to 1000 L)
- aerobic fermenters for pertussis fermentation with special stirrers and mechanical foam breakers
- equipment for yeast fermentation and for the state-of-the-art production of antigens such as Hepatitis B Antigen (HBsAg)
- viral cell culture systems for polio, rabies and foot and mouth disease (FMD), for example.

These production lines are complemented with supplementary tanks for media preparation and harvesting, for example, and further enhanced by integrating downstream process equipment such as cell and product separators, homogenizers for cell disruption and/or filtration units for microfiltration and ultrafiltration.

The integration of special separators and filter systems enables cell debris removal and chemical–based virus inactivation. Further purification steps such as chromatography are managed by integrating equipment from third-party suppliers.

The final step in vaccine production is formulation, which is also in GEA’s scope of supply. Inactivation systems for waste and effluent treatment can also be supplied. Automation is achieved using PLC or DCS systems, which can be incorporated into appropriate SCADA or MES infrastructures.

**GEA’s Vaccine Technologies**

- Fermentation
- Mechanical separation
- High pressure homogenization
- Media preparation and formulation
- Freeze drying or aseptic spray drying
- Inactivation and waste treatment
The GEA Advantage
A critical factor underlying the success of the company is its ability to swiftly translate new developments into marketable processes and systems that fully meet the complex requirements of biotechnological procedures.

GEA is a single-source supplier of modular systems and solutions to meet the needs of any pharmaceutical, microbial or cell fermentation process. The company has the expertise and industry knowledge to help customers test processes and make the right choice of equipment to ensure security of outcome and the fastest time to market.

All vessels can be supplied as standalone equipment or as automated process units delivered as fully functional modules, installed on site, including agitators, homogenizers, metering and regulating technology, control units, valves and pipe connections. Options for hazardous environments are also available.

Quality Credentials
- cGMP/FDA/EMA
- Manufactured as per PED (Pressure Equipment Directive)
- ASME U-Stamp
- China Manufacture License (SELO)
- Quality plan and materials tracing
- Own non-destructive testing
- Weld seam documentation
- Qualification (IQ/OQ)
- Quality Management System according to DIN EN ISO 9001.

PERTUSSIS FERMENTATION SYSTEM FOR TIANTAN BIO
Vaccines are among the 20th century’s most successful and cost-effective public health tools for the prevention of disease, disability and death. Vaccination not only protects individuals, but also entire communities from diseases spread by person-to-person transmission.

Fueled by new product introductions and rising usage in many regions around the world, the global market for vaccines has experienced strong growth in recent years, particularly in Asia.

Beijing Tiantan Biological Products Co. Ltd (Tiantan Bio) operates as a subsidiary of the National Vaccine and Serum Institute (NVSI) and is primarily engaged in the research, development and production of bacterial and viral vaccines, blood derivatives, diagnostic reagents and various biopharmaceutical products.

Needing a new fermentation system, the company contacted GEA. After several site visits and a period of close collaboration, a quote was prepared that resulted in Tiantan Bio ordering a fermentation system from GEA in Germany. Detail engineering work soon began: the system comprises two seed fermenters (50 and 500 L), two 5000 L production fermenters and a CIP system.

Now installed and operational, Tiantan can add Acellular Pertussis Combined Vaccine Adsorbed to its portfolio of products and help a multitude of people to live better, safer and healthier lives.
Our engineers work closely with our clients to develop complete solutions — for applications such as vials, ampules, infusion bags, drops, and sprays — that are individually tailored to specific project requirements, including automation packages and software development.

All engineering, manufacturing, qualification and plant documentation is, of course, FDA, EMEA and GMP compliant.

Also, GEA offers plant for the formulation of syrups, suspensions, and parenterals. Systems for the production, storage, and distribution of clean utilities and media complete the portfolio.

Pharmaceutical Freeze Drying/Lyophilization
GEA is one of the market leaders in pharmaceutical freeze drying/lyophilization and automatic loading and unloading systems. With more than 60 years of development, engineering and manufacturing experience and a pedigree of more than 1000 freeze dryer installations worldwide, GEA is a reliable supplier of high quality aseptic production solutions.

ISO 9001 certified and fully compliant with cGMP, GAMP and other relevant guidelines, GEA supplies a comprehensive range of products and services, comprising laboratory freeze dryers for pilot-scale, R&D and small production batches, industrial freeze dryers and complete freeze dryer systems.

These include vial conveyer systems, Automatic Loading and Unloading Systems (ALUS™), integrated isolators and CIP skids with integrated freeze dryers.

Our expertise includes innovations in shelf, chamber, slot door and condenser design, novel technologies to minimize plant footprint and decrease energy use, save costs and reduce cycle times, and a fast-track approach to full project execution — from signed contract to SAT in less than 9 months.

GEA offers a complete program of high quality products associated with all aspects of aseptic manufacturing and integrated solutions, in addition to efficient service for the pharmaceutical, healthcare and biotech industries.

Spray Drying
For expensive sterile drugs, shelf-life is critical. The traditional way to convert a sterile liquid into a stable solid form is freeze drying; but, now, there’s an alternative. Spray drying is rapidly becoming the preferred technique for a growing number of pharmaceutical companies to produce better drugs.

This ultrafast, continuous and gentle drying technology offers unique ways to define particle characteristics and enable the development of novel formulations and delivery systems that were previously unattainable.
TOTAL VIAL TRACEABILITY
In collaboration with SCHOTT and HEUFT, GEA has developed a vial traceability solution that will help the pharmaceutical industry to implement the EU’s drug anticounterfeiting directive, safeguard the rights of trademark and patent holders and, ultimately, protect patients.

The clock is ticking! The European Commission’s Directorate General for Health and Food Safety will soon be implementing the Falsified Medicines Directive. Pharmaceutical manufacturers now have limited time to meet the requirements of the new legislation and ensure the end-to-end verification of drug authenticity.

Whether it’s a fad or the future, 100% vial traceability is becoming an increasingly important consideration in the pharmaceutical freeze drying industry. The current situation is that traceability can only be done at batch level, which provides very little information about the time, position or condition (weight, for example) of a vial. Essentially, all vials are equal and anonymous. The ideal situation is that “every vial has a name” and can be individually tracked and traced.

Continuous Monitoring and Full Traceability: LYODATA™
A new type of system for the continuous traceability of primary packaging, including complete process and product data backup, could provide the ideal solution. LYODATA™ provides unique marking, clear identification and the consistent traceability of pharmaceutical primary packaging, making drug counterfeiting practically impossible. The system also offers continuous quality inspection, 100% line clearance and precise sampling.

Ensuring distinctive and unmistakable marking and the 100% traceability of pharmaceutical products in vials or containers by laser coding and code verification, the system also includes process and product monitoring data from primary packaging production, grading and freeze drying, right up to the final finished product!

Unique Marking and Clear Detection
SCHOTT technology is used to laser mark a 2D barcode onto the glass vial or bottle during production. HEUFT’s innovative all-round code verification system, which is fully compatible with GEA’s Automatic Loading and Unloading System (ALUS™) and suitable for oRABS, cRABS and isolator use, then checks the (GS1) coding. Loading speeds of up to 500 vials per minute are achievable, with each vial being subjected to a full examination both before and after lyophilization.

With the ultimate aim of guaranteeing a unique identification code for each sample, tracking it during the freeze drying process, having real-time access to the data and vials in process and to be able to document that data for customer use, GEA has made a commitment to 100% vial traceability. This not only prevents drug counterfeiting and protects intellectual property, it also helps to uphold the health of the patient.
Processing Blood

GEA uses its experience and expertise to unite a range of technologies to create complete processing plants for blood and plasma processing, including controlled precipitation, centrifugation and filtration for solid/liquid separation, thermal and chemical inactivation, ultrafiltration/diafiltration, nanofiltration, chromatography and precise temperature control.

GEA supplies plant and components for fractionation, concentration, pre- and post-virus inactivation, purification and buffer production, storage and distribution. In addition, depending on the application, plasma may need to be frozen to –30 °C within 60 minutes; GEA can supply equipment to accurately maintain such extreme low temperatures.

An essential part of high-quality blood plasma production is an integrated CIP/SIP system. GEA provides efficient cleaning and sterilization processes that meet your individual demands and ensure that sterile media is delivered to the right place at the right time. We offer a wide range of cleaning options, from mobile, independent cleaning systems to CIP satellites fed with conditioned cleaning solutions.

We integrate GEA's proven hycon separators to enable fully automatic discharge, which saves time and makes the process safer for both the product and the operator. Designed for CIP and SIP applications, sterile handling is guaranteed during the entire fractionation process under cooled conditions.

Whatever you need your process plant for — from the fractionation and manufacture of products such as immunoglobulins or human albumins to Factor VIII/Factor IX — our wide range of plant concepts will provide for any task to be performed in a safe and cost-effective way and take account of any specific requirements or conditions.

The company has successfully planned and built plants for plasma fractionation all over the world.

**Essential Process Requirements**

- Gentle thawing of the plasma by precise temperature control and regulated stirring
- Appropriate conditions for solid/liquid separation by centrifugation or filtration to separate the plasma fractions
- Special filtration techniques to obtain eluate for the manufacture of Factor IX
- Exact temperature control for the precipitation of all fractions
- Optimised sterile design
- Compliance with emission regulations when dosing the precipitation medium.
STATE-OF-THE-ART IMMUNOGLOBULIN PRODUCTION

GEA was responsible for the installation of a new immunoglobulin (IgG) manufacturing plant, including detail design engineering, for an annual capacity of more than 3 million liters of PEQ (plasma equivalent).

The whole procedure starts by suspending the precipitate to produce the final formulated bulk, including the integration of several different treatment and virus inactivation steps — depth filtration to remove protein contaminants, anion exchange chromatography to deplete residual impurities, dia/ultrafiltration to remove process residuals and to concentrate the protein and/or nanofiltration to remove very small particles — all fed using 32 high quality GEA pharmaceutical product and buffer tanks (1000–8000 L).

Through continuous improvements of the P&IDs (Process & Instrumentation Diagrams) during the detail engineering phase, the latest technological advances have been integrated into the immunoglobulin production process.

As well as various maintenance and ease of operation aspects, special attention has been paid to the capacity of individual plant areas, allowing future potential development in terms of output and yield. The highly automated process ensures lot-to-lot consistency and product quality.

Full automation of the plant, including the cleaning and sterilization processes (CIP, SIP), ensures that the plant can operate almost autonomously. The result is an efficient manufacturing process and plant that's based on the highest technological, viral safety and purity standards, which will give patients the confidence and peace of mind that they are receiving high quality immunoglobulin products.
At a Glance: LIQUIDS Solutions

Applications

- Animal Cell Cultures
- Antibiotics
- Bacterial Cultures
- Blood Fractionation
- Hormones & Steroids
- Inhalable Suspensions
- Insulin
- Liposomes
- mAbs
- Oncology Drugs
- Parenteral Intravenous Emulsions
- Therapeutical Proteins
- Vaccines

Core Technologies

- Distillation & Fermentation
  - Fermentation
- Homogenization
  - Cell Rupture
  - Micronization
  - Emulsification
- Separation
  - Liquid-solid Clarification
  - Liquid-liquid Separation
- Membrane Filtration
  - Nanofiltration
  - Ultrafiltration
  - Microfiltration
- Liquid Processing
  - Continuous Blending
  - Inline Mixing
  - Media Preparation & Formulation
  - Mixing & Blending
- Product Handling
  - Containment
  - Dispensing & Dosing
  - Fill & Finish
  - Loading/Unloading
  - Storage
- Drying & Particle Processing
  - Spray Drying
  - Freeze Drying
  - Lyophilization
Integration experts

- Analytics, Monitoring & Process Control
- Process Integration
- Cleaning & Sterilization
- CIP/SIP Technology

Utilities

- Air Conditioning & Chilling
- Cooling & Refrigeration
GEA Group is a global engineering company with multi-billion euro sales and operations in more than 50 countries. Founded in 1881, the company is one of the largest providers of innovative equipment and process technology. GEA Group is listed in the STOXX® Europe 600 Index.