



Making Science Work

Pharmaceutical processing solutions
for solid and liquid dosage forms



Working Together to Make a Difference

GEA has developed a deep and thorough understanding of the challenges you face, the hurdles you need to overcome and the goals you want to achieve

A well-established expert in the pharmaceutical manufacturing industry, with the knowledge derived from thousands of successful installations, all over the world, GEA is the trusted partner of choice for clients and customers, both large and small, who want to go further, faster, and develop process-related solutions for a wide variety of applications and products.

No matter where you are, whatever the scale of your operation or indication, we have the capability to make your concept a reality, optimize your process, improve your production efficiency and deliver the ongoing support to make your business a success.

Relationships matter, and we believe that by giving you access to the scientists and engineers who actually created our equipment and developed our technologies, you can invest with confidence, safe in the knowledge that GEA plant is designed to achieve its maximum potential and has been optimized for manufacturing excellence.

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.

By delivering everything from technical know-how and process evaluation support to product development, expert-designed equipment, project management and the service you need to bring your plans to fruition, we supply the added value and the deep-rooted knowledge that counts.

GEA is your single-source supplier of robust, flexible and cost-effective manufacturing solutions that maximize operational reliability and productivity. From batch and continuous granulation, drying and coating to contained materials handling, tablet compression, freeze drying, fermentation and separation, and from blood processing, mAbs and MUPS to effervescent OSDs and vaccines, we offer the largest variety of process technologies and boast an unrivaled history of identifying the most appropriate solution for your specific application.

Whether it's a single piece of equipment or a long-term strategic collaboration, our focus is on price-performance leadership, safety and quality. How do we do this? By making science work.

Solutions for Solid Dosage

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 your productivity.

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

- highly potent APIs
- inhalable fine powders
- MUPS tablets
- effervescent
- multilayer pellets and tablets
- hormones.

FDA EMBRACES THE BENEFITS OF GEA'S CONTINUOUS TECHNOLOGY

Staying true to its mission of ensuring that safe, effective and high quality drugs are available for the American public, the US Food and Drug Administration (FDA) has recently purchased a GEA ConsiGma® 1 oral solid dosage development unit to conduct further research into continuous manufacturing.

Housed in the agency's CDER/VOPQ (Office of Pharmaceutical Quality), the "important asset" will be used by the Testing and Research and Emerging Technologies Team to support the development and adoption of novel technologies and modernize pharmaceutical processing and manufacturing.

The GEA ConsiGma® 1 combines QbD principles with DoE to explore and optimize a wide range of process parameters with less product in a shorter timeframe, resulting in a better understanding of continuous manufacturing.

As such, research scientists and engineers can introduce cost-effective strategies that meet the pharmaceutical industry's demands for faster product development, improved production economics and increased manufacturing flexibility.

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.



GEA AND RCPE TO SUPPORT PHARMA'S ADOPTION OF CONTINUOUS MANUFACTURING

Combining GEA's fully integrated continuous manufacturing lines with RCPE's expertise in simulation, modeling and material science will facilitate the industrial implementation of advanced production technologies

GEA, a trusted supplier of advanced engineering services and process equipment, and the Research Center for Pharmaceutical Engineering GmbH (RCPE) — established as one of the Competence Centres of the Austrian COMET-Program and owned by the Graz University of Technology, University of Graz and Joanneum Research GmbH — experts in process and product optimization, are working together to help pharmaceutical and life science companies implement continuous manufacturing lines to produce oral solid dosage (OSD) forms.

The GEA-RCPE partnership provides a single-source repository of process technology and design know-how and material science, as well as simulation and modeling expertise, to optimize the integration and functionality of production-scale process technologies and unit operations. Aiming to improve product development and help pharmaceutical companies to better negotiate the regulatory submission process, the companies hope to shorten timelines, reduce risk and expedite drug development from R&D through tech transfer to commercial manufacturing.

"GEA has pioneered the development of cutting-edge technologies to bring continuous manufacturing (CM) to the pharmaceutical industry. With our unparalleled history of expertise in processing OSDs, from pills to pellets to MUUPS, and our tried and tested technologies, I am convinced that we can continue to help our customers to get their products to market faster in a cost-effective way," said Phil Gabb, Head of Solid Dosage Sales Support.

RCPE's main focus is on the development of new drug delivery systems and the associated production processes and their monitoring. Application-oriented research and development projects are done in collaboration with industrial and scientific partners to facilitate the implementation of CM systems.

Massimo Bresciani, Executive Director, Business Development and Scientific Operations, RCPE, said: "We are proud and energized to collaborate with GEA. It's a unique opportunity to further expand our remit in the area of advanced manufacturing science and, specifically, in CM. By combining our experience and industry presence, GEA and RCPE can more effectively support pharmaceutical companies to adopt innovative CM solutions and meet their regulatory requirements."

Frans K.A. Maas, Vice President for GEA's Pharma Solids business, added: "The collaboration with RCPE is another step towards expanding our ecosystem, de-risking the migration from batch-based to continuous processing and delivering added value to the pharmaceutical sector. By working with academic organizations such as RCPE, our ultimate aim is to get safer medicines to market in a more efficient and cost-effective way so that everyone has access to the most efficacious pharmaceuticals, wherever they are in the world."



Batch Processing

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.



Single-Pot processing



AirConnect® for flexible small-scale processing

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 the most important unit operation 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. Whereas the use of a high shear granulator with a fluid bed dryer is still the most widely used combination, offering both high levels of productivity and versatility — particularly for large volume products and long campaigns — there are a number of granulation technologies available to pharmaceutical manufacturers.

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 plant for cGMP production that is configured to meet the customer's specific requirements.

Integration by Design

Designed and built with integration in mind, our modular systems enable customers to select from a wide variety of equipment to meet their granulation and drying requirements. We supply entire turnkey installations, including fluid bed process machinery combined with top- and bottom-drive high shear mixer-granulators, as well as integrated contained materials handling, wet and dry milling facilities, product handling systems, binder and coating preparation units, filtration units and rotary tablet presses.

Plus, based on the established combination of a single control unit with a diverse range of process modules, our innovative plug and play technology, PharmaConnect®, provides the opportunity to process formulation batches from 5–60 kg. It can also accommodate 1:10 scale-up procedures that are completely compliant with current regulatory requirements. Integrating GEA's BUCK® containment valve solutions further enhances the system's capabilities.

Whatever your application, whether it's high shear granulation or inhalation blending, extrusion and spherization or IBC blending, safety, containment, product flow and building requirements are in-built for full integration and optimum process efficiency.



Tableting

Tablet Compression

As a single-source supplier of 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 while varying the machine speed 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.



The MODUL™ Q rotary tablet press

Tablet Coating

The ConsiGma® coater from GEA is a revolutionary, new, high performance tablet coating technology that gently and accurately deposits controlled amounts of coating materials on tablets — even if they are extremely hygroscopic or friable.

Designed specifically to be an integral part of the ConsiGma® continuous tableting lines, the ConsiGma® coater is able to process small quantities of tablets at very high rates, offering improved heat and mass transfer.

PAT-compatible, the ConsiGma® coater is easy to clean and offers significant cost savings compared with conventional systems in terms of time, materials, downtime, process revalidation, stability testing, etc.

With a smaller technical space requirement than established technologies, less cleaning and a reduced plant area is needed. And, being a continuous production technology, no scale-up is required and the maximum batch size is almost infinite.



The ConsiGma® coater



Continuous Processing

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 plant 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.





The implementation of CM enables a more efficient way of making drugs and moving away from stepwise and time-consuming batch processing to 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 a traditional plant. 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 plant increases the chance that local manufacturing sites can be established to meet regional needs and so reduce global transport requirements.

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.

Looking to the Future

GEA has been successfully demonstrating its late-stage development-to-manufacturing capabilities for many years. With the portable, continuous, miniature and modular (PCMM) pod-based mini factories, for example, GEA and its partners are leading the way toward smaller, more flexible, continuous processing technologies that have the potential to transform the future of pharmaceutical development and manufacturing — and deliver customized quantities of drugs to patients in need in a quick and efficient way.

With 14 years of continuous learning, GEA has firmly established its longevity in the CM market. And having completed more than 70 projects involving a variety of filed and authorized products, including the first ever FDA-approved breakthrough therapy developed and manufactured using the ConsiGma® platform, no other company has as much experience and done more to pioneer continuous manufacturing for the pharmaceutical industry.

Contained Materials Handling

GEA is a trusted supplier of materials 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 fuse performance excellence with technological innovation to deliver long-term competitive advantages.

Our comprehensive portfolio of standard and custom designed equipment, machinery and entire production lines ranges from benchtop R&D solutions to completely integrated industrial-scale plant and continuous processing technology.

Using well-established and proven components, we can supply both simplicity and flexibility in plant design. User-selected process options, cleaning equipment, control systems and PAT technologies combine to meet process requirements exactly. This approach ensures that qualification and validation procedures are kept to a minimum.

And, 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.

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.

The GEA Approach

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.

Yet, 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. Even for the most challenging products, including potent APIs, MUPS tablets, effervescent and multi-layer pellets, we 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.

GEA not only offers the largest variety of robust and compliant hardware solutions for contained materials handling, we've also developed an unrivaled level of expertise when it comes to identifying the most appropriate solution and a thorough understanding of containment risk analysis.

We provide tailor made containment for the pharmaceutical industry — for now and for the future.





For visibly contained product transfer and the safe handling of potent products, the disposable Hicoflex® system is quick and easy to install and use



GEA can supply an entire, completely integrated containment system, from raw material to coated tablet

The BUCK® MC Lite is the lightest split butterfly valve for the contained transfer of highly potent solid dosage products





CONSIGMA® CDC 50 COMPLETES 120 HOUR TRIAL RUN

In conjunction with MSD, a tradename of Merck & Co., Inc., we've recently completed an extended trial run to assess the robustness of our ConsiGma® CDC 50 Continuous Direct Compression system at the GPSC. By the end of the 120-hour trial, more than 15 million tablets had been made using approximately 6200 kg of raw material in a single production area. Importantly, final analysis indicated that the campaign length could be increased even further and run for longer.



GEA Pharma Solids Center

Offering a full range of batch and continuous manufacturing technologies for the testing, development and optimization of oral solid dosage forms

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 a comprehensive assortment of tableting technologies, from powder handling to granulation, 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 Compact 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.

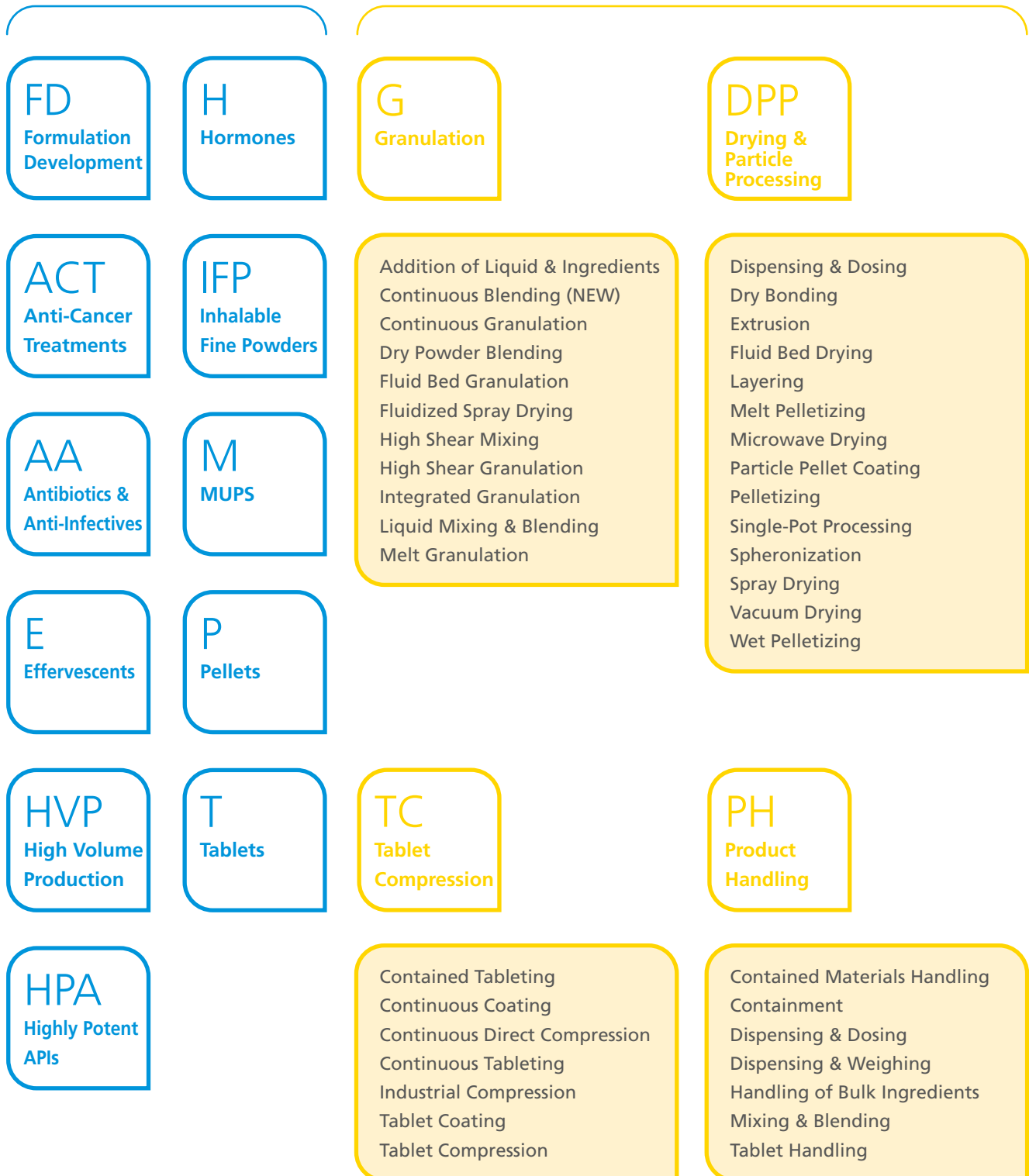
To discover more or organize a test, demonstration or training session, contact our dedicated, passionate and experienced team. With a long history of solid dosage form expertise, including more than 125 formulations on CM equipment, everyone at the GPSC is committed to going the extra mile to meet customer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



At a Glance: Solid Dosage Solutions

Applications

Core Technologies



Integration Experts

A

Automation

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

U

Utilities

Air Conditioning & Chilling
Cooling & Refrigeration

S

Service

Getting You Started
Keeping it Running
Constantly Improving
Together with You





Processing Pharma Liquids

GEA supplies integrated process systems for the production of liquid dosage and biopharm products for the pharmaceutical and biotechnological industries

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.

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.

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.

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.

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
- Welding documentation
- Qualification (IQ/OQ)
- Quality Management System according to DIN EN ISO 9001.

Integrated Solutions for Pharma Liquids

With a proven track record in API processing and liquid dosage form production, GEA's primary and secondary manufacturing systems provide the quality, reliability and efficiency you can depend on.

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 plant 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.

Pressure rated process vessels from GEA set new performance standards and ensure that our customers' central process components have competitive advantages. The surfaces of our process vessels, fermenters and bioreactors 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 tanks for pharmaceutical fermentation processes.

Separation

Pharmaceutical biotechnology requirements are high, including aseptic process management, optimum cleaning capability, closed product handling, reliable compliance with GMP requirements, 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.



GEA has been instrumental in advancing mechanical separation technology. Offering solutions in areas such as monoclonal antibodies, insulin, vaccines, starter cultures, human blood plasma and enzymes, the company's technology plays a key role in the recovery of APIs and optimizing production processes and products.

With standalone machines and sophisticated skid designs that guarantee a high yield of valuable substances, and operate trouble-free, efficiently, reliably and economically throughout a long service life, GEA has developed numerous innovative improvements to separating processes.

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.

After years of development, GEA has provided two insulin production lines, including centrifugal separators, fermenters, flow components, high pressure homogenizers, a significant number of valves and engineering support. The multimillion Euro order was scheduled for completion during 2017 and further reinforces the co-operative business relationship between the two companies.

The order from Hanmi comprises equipment for two identical fermentation and media preparation lines, fully equipped with 7000 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; Hanmi has designated the VESTA® range as its standard valve technology.

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.

Integrated Solutions for Pharma Liquids

High Pressure Homogenization

Cell Disruption: High-pressure homogenization is widely used in cell rupture (cell rupturing, cell disruption) applications to extract intracellular compounds (sometimes without using solvents or other chemicals to break the cell wall). Being very effective and efficient, the homogenizers can often maximize the yield from valuable source material while keeping product quality at a very high level. 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. The ability to micronize particles down to the nanometer range improves the stability of active ingredient dispersions and enhances their clinical effectiveness. Optimized particle micronization and homogenous distribution means that, even in intravenous emulsions, API bioavailability and drug tolerance is improved.



Membrane Filtration

Membrane filtration offers tremendous separation and purification opportunities to the pharmaceutical and biotechnology industries, resulting in significant advancements in both product development and quality. GEA specializes in cross-flow membrane filtration — microfiltration, ultrafiltration, nanofiltration — and reverse osmosis. Along with our process experience, we offer a wide range of both polymeric and inorganic membrane systems to provide the best possible solutions to our customers in the biotechnology industry.

Membrane filtration for cell harvesting or biomass recovery is an important step in any fermentation process, especially when manufacturing bulk intermediates such as antibiotics. Membrane filtration can successfully replace separation methods such as rotary vacuum filters or centrifugation in many facilities by significantly improving product yields and reducing operator involvement and maintenance costs. Membranes are also a standard part of industrial enzyme manufacturing lines to concentrate the enzymes prior to further downstream processing.

Flow Components

From components to equipment and complete process lines, GEA offers a wide range of liquid handling solutions for use in pharmaceutical production plants.

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 that includes valve technology for all hygienic classes (Hygienic, UltraClean, Aseptic), hygienic pumps and cleaning technology.

Our components are designed to meet the highest requirements and can be readily combined with our standardized modular plant. Contact us today for more information about pumps, valves, cleaners, inline process connections, tank safety systems and expansion compensators.

GEA CROSSES THE FOOD-PHARMA DIVIDE WITH KOREAN TPN PROJECT

Celebrating GEA Pharma China's first overseas project, the company has installed a formulation process system in JW Life Science's Dangjin facility to produce TPN products

Wishing to expand its total parenteral nutrition (TPN) production capabilities, JW Life Science (JW), a leading Korean pharmaceutical company that specializes in infusion solutions, contacted GEA. After a year of discussions to define the scope of supply, a contract was signed to deliver 11 core process skids, one CIP skid and one GEA homogenizer. With a long history of implementing both food and pharma plant, GEA was more than qualified to provide the right level of technology and equipment.

To reduce the project timeline, the skids were built and pre-assembled before being sent to Korea for on-site installation. This not only accelerated the commissioning process, it also reduced construction costs and minimized the risk potential.

The project was particularly noteworthy because, in accordance with JW's global vision, the design, manufacture, installation, documentation and validation of the project are completely GMP- and FDA-compliant. The formulation system, including GEA's homogenizer, is fully integrated, reducing the project management interface.

Furthermore, the automation system offers full redundancy to minimize failure rates and improve production safety, and can be interfaced with JW's MES system to form a unified production formula and order mode.

Impressive Results

Delivered in record time, advanced project management, fluent bilingual communication and excellent teamwork all played an important role. GEA China has more than 15 years of experience in the field of pharmaceutical formulations and benefits from both international project experience and specialized training.

Like many other customers, JW recognized that whatever the application — whether food, pharma or even a combination of the two — GEA has the technology, the know-how and the global presence to provide the perfect blend of equipment, expertise and guidance to meet those requirements.

Integrated Solutions for Pharma Liquids

Pharmaceutical Freeze Drying/Lyophilization

GEA is one of the market leaders in pharmaceutical freeze drying/lyophilization. With 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 technology to avoid sticking stoppers, minimize footprint and energy usage, sterilization technology to 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.

LYOSPARK® Nucleation Technology

LYOSPARK® controlled nucleation technology from GEA facilitates uniform ice crystal formation in laboratory and production-scale freeze dryers with a minimum degree of supercooling. This is reflected in more consistent and larger ice crystal sizes with a more open product structure. As a result, faster drying and reconstitution times can be achieved. In addition, LYOSPARK® ensures inter-batch homogeneity, improves process repeatability and enhances both the presentation and quality of the final product.

LYOSENSE® Online Moisture Control

Based on multipoint NIR measurements, the LYOSENSE® online moisture sensor from GEA comprehensively and non-destructively evaluates freeze dried product cakes in real-time. This easy-to-install and use measuring device is a non-invasive solution to moisture control, enabling the effortless detection of residual moisture, glass particles, cake homogeneity and API concentration. Fully GMP and 21 CFR Part 11 compliant, and supplied with IQ/OQ/PQ support, the LYOSENSE® needs no consumables and provides the following benefits: whole cake assessment; fast processing times (5 ms); and a simple operator interface.

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 (ALUSTM) 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.

"The pharmaceutical and biotech industry has long been looking for a solution," says GEA's Johannes Selch, adding: "Manufacturers needed to progress from a batch-based system to achieve precise vial control and traceability during the entire sterile production process. Now, there's no more hide and seek, any vial can be located at any time or process step. It's a simple case of 10,000 vials in and 10,000 vials out."



Whether it's a fad or the future, 100% vial traceability is becoming an increasingly important consideration in the pharmaceutical freeze-drying industry



ALUS™ ISOLATOR AND BARRIER SYSTEMS

Isolator-based aseptic processing evolved in the pharmaceutical industry as the need to separate the operator from the “critical zone” and reduce product risk became increasingly important.



Barrier and isolator systems are widely used in a number of industries; in pharmaceutical processing — from sterile injectable drug filling to cytotoxic sterile drug compounding — they are primarily employed to maintain the sterility of a drug product.

Application-Specific Systems

Our extensive portfolio of products, technologies and services includes complete plant and components for the manufacture of

- insulin
- monoclonal antibodies
- blood-derived products
- vaccines.

This includes systems and plant for the production, preparation and storage of media and clean utilities, fluid management, fermentation, cell cultivation and purification.

Liquid Dosage Oncology Products

As a result of growing competition and more stringent regulatory requirements for end-user safety, improving the convenience and ease of administration of parenteral therapeutics is becoming a common strategy for biotechnology and pharmaceutical companies. Manufacturers wishing to gain market share and provide high quality products for healthcare professionals and cancer patients alike are increasingly investing in the development and delivery of liquid dosage forms, freeze-dried products and injectables.

Pharmaceutical Development

GEA is known all over the world for its individual and tailor-made process plant for the manufacture of free-flowing pharmaceutical and biotechnology products. Complete plant, modular equipment, process units and skids can be assembled, tested and qualified in our own production facilities. We perform tests and trial runs with appropriate media to demonstrate the functionality of all components and equipment before the plant is delivered.

In collaboration and partnership with our customers, we aim to develop and deliver high-performance plant and economic process systems that comply with the highest operational safety and environmental standards; we want our customers to use our groundbreaking solutions to manufacture even better products in the future.

GEA can supply a specialized, contained and fully integrated system when no standard off-the-shelf one exists, particularly for toxic or highly potent drugs such as cytostatics or echo contrast media. With our innovative ideas and fresh approaches, together with your project team, we will find a solution that's tailored to your needs — from basic engineering to fabrication and qualification.



Insulin

GEA has a proven history of successfully installing plant for the production of insulin, including the engineering, delivery, commissioning and qualification of entire ultra-pure media systems as well as various process equipment and cleaning installations.

A worldwide technology leader in insulin production, GEA is able to supply the clean utility systems and manage the integration of all the main processes, including fermentation, harvesting, chromatography, filtration and freeze drying.

The biosynthetic production of human insulin is done using bacteria or yeast cells. Following fermentation, the biomass is separated (at a constant concentration) by a nozzle separator, washed, concentrated and homogenized to release the insulin. The raw insulin is then treated and precipitated to produce crystals.

Centrifuges and process lines provided by GEA have an established pedigree in the clarification, separation, classification, concentration and fractionation steps. We supply process-specific chamber and nozzle separators and machinery for use in the subsequent crystallization stages.

Monoclonal Antibodies (mAbs)

GEA offers production systems for mAbs that are produced in state-of-the-art stainless steel bioreactors by specific cell cultures. mAbs are known as targeted therapies because they work by selectively binding to specific proteins on the surface of cells.

Driven by demand, the approval of new products and the launch of generic mAb drugs, they have been successfully used to treat cancers, tumors and other serious diseases, such as auto-immune disorders. Compared with other biopharmaceutical products, monoclonal antibodies are large proteins that, traditionally, necessitate high-volume manufacturing equipment/systems and facilities.

The cell culture process is done in several steps, starting with low-volume precultures and successively cultivating intermediate batches of, for example, 40, 200, 1000 and 5000 L, to the final production volume of up to 20,000 L. These systems comprise the vessel, with the stirrer as the core element,

and peripherals such as temperature control systems, CIP components, aeration and deaeration systems, dosing systems and automated sensors, actuators and the operator interface.

Support processes such as media preparation and harvest systems are also available at GEA. The process integration of separators and filters for the harvest step is also within GEA's scope of service.

As mAb fermentation is a long process, and because of the high sensitivity of the cells — and the need for operator and product safety — all system components are designed according to the latest standards and have the highest grade of finish quality.

Pharmaceutical Proteins

Proteins with pharmaceutical and analytical applications, such as hormones and enzymes, are produced by mammalian cell culture or by the cultivation of recombinant yeasts or bacteria.

Extracellular products: After fermentation, the micro-organisms are removed by continuously operating separators. To increase the yield, the solid material is washed and extracted by centrifugation. The clarified phases of the two stages are mixed and fed to further stages of the process, such as precipitation or separation, for example.

Intracellular products and inclusion bodies: In intracellular processes, the required product may be contained in the intracellular liquid or in so-called inclusion bodies. In contrast to extracellular bioproduction, the clarified phase leaves the process here and the biomass is processed. The washed and concentrated biomass is homogenized — the cells are broken down and the intracellular liquid or the inclusion bodies are released.

These are separated from the cell fragments, washed and concentrated in further stages of the process by centrifuges. For intracellular products derived from the cytoplasm, the solids are precipitated and removed by continuously operating separators. Further product concentration may be done by chromatography.

To keep the process as simple as possible, the biomass is sterilized directly after fermentation in the fermenter by heat or by chemical methods.

Processing Vaccines

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.

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.

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 (NCSI) 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.

Gentle Blood Processing

GEA uses its experience and expertise to unite a range of technologies to create complete processing plants for blood 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 plant 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
- Optimized 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: Liquid Processing Solutions

Applications

ACC Animal Cell Cultures	L Liposomes
A Antibiotics	M mAbs
BC Bacterial Cultures	OD Oncology Drugs
BF Blood Fractionation	PIE Parenteral Intravenous Emulsions
HS Hormones & Steroids	TP Therapeutic Proteins
IS Inhalable Suspensions	V Vaccines
I Insulin	

Core Technologies

DF Distillation & Fermentation	LP Liquid Processing
Fermentation	Continuous Blending Inline Mixing Media Preparation & Formulation Mixing & Blending
H Homogenization	
Cell Rupture Micronization Emulsification	PH Product Handling
S Separation	Containment Dispensing & Dosing Fill & Finish Loading/Unloading Storage
Liquid-Solid Clarification Liquid-Liquid Separation	
MF Membrane Filtration	DPP Drying & Particle Processing
Nanofiltration Ultrafiltration Microfiltration	Spray Drying Freeze Drying Lyophilization

Integration Experts

A

Automation

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

U

Utilities

Air Conditioning & Chilling
Cooling & Refrigeration

S

Service

Getting You Started
Keeping it Running
Constantly Improving
Together with You



GEA Service – For your continued success

GEA Service partners with our pharma and biotech customers, supporting them throughout the entire lifecycle of their plant and equipment to ensure business success. To guarantee optimum performance and operational excellence, we provide a wide range of services to maintain and improve your plant and equipment.

Getting you started: seamless support for instant productivity and performance

From installation onwards, our GEA Service teams will work with you to get the best out of your plant and equipment. As a supportive and committed partner for life, we start as we mean to go on.

We plan and build according to individual needs, sharing process knowledge, training staff and supporting operators to get you up and running and deliver a smooth, seamless and ongoing service for optimum performance and safety.

Keeping it running: the cost-efficient way to ensure safety and reliability

Regular maintenance is not a cost, it's an investment. By implementing corrective and preventive maintenance techniques, we ensure high performance, availability and quality — as well as maximizing the lifecycle of your equipment or plant.

To ensure you benefit from continuous production and minimal downtime, we provide fast support and top quality spare parts, whenever and wherever they're needed.

Constantly improving: sharing our knowledge to safeguard your investment

To meet your production requirements — today and tomorrow — GEA works with you to keep your equipment up to date and optimized.

We safeguard your investments by constantly looking ahead, by upgrading or modernizing equipment and enhancing processes to meet changing needs and new market demands. We are always working to increase production efficiency and ensure peak performance.

Together with you: enduring commitment to you and your business

By integrating the latest automation and control solutions, we boost your output and efficiency, reduce waste and minimize both resource use and the need for manual intervention.

Our commitment to you and your business means investing in your objectives, your risks and your future success. We collaborate with you to provide ongoing systems audits and on-site support, and to generate improved performance through innovative new service models.

Virtual technology improves productivity and reduces downtime

KEEPING IT RUNNING



FOR BETTER BUSINESS SUCCESS

GEA Service partners with our pharma and biotech customers, supporting them throughout the entire lifecycle of their plant and equipment to ensure business success.



We live our values.

Excellence • Passion • Integrity • Responsibility • GEA-versity

GEA is a global technology company with multi-billion euro sales operations in more than 50 countries. Founded in 1881 the company is one of the largest providers of innovative equipment and process technology. GEA is listed in the STOXX® Europe 600 Index. In addition, the company is included in selected MSCI Global Sustainability Indexes.

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