GEA Granulation Technologies

Multipurpose Process Solutions for Solid Dosage Forms
**GEA Group** is a global specialist in solid and liquid dose technology. Combining trusted technology with an ongoing programme of innovation and price/performance leadership, GEA has a long history of expertise and an unparalleled depth of experience in the fields of batch and continuous granulation, drying, pelletizing and coating, contained materials handling, tablet compression, pharmaceutical freeze drying, fermentation and liquid formulation, separation, homogenization and cell disruption.

With manufacturing and technology centres all over the world, GEA provides the services that the pharmaceutical industry needs, including technical know-how, test facilities for product development and process evaluation, project management, market-leading equipment, customer service and support.

Working closely with its customers to develop new products, reduce time to market and enhance clinical effectiveness, GEA’s scope of supply ranges from R&D-scale and standalone production equipment to the installation of completely integrated production lines and continuous processing technology. GEA is your single-source supplier of robust, flexible and cost-effective pharmaceutical manufacturing solutions that maximise operational reliability and productivity.
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 prior to 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 not fully understood and the selection of a particular machine and granulation method is frequently done on the basis of tradition and the operator’s own experience, rather than by using strict scientific or cost-benefit criteria.

The basic techniques have evolved in recent years and granulation for controlled release, extrusion, spherization, fluidization techniques, spray drying, melt extrusion, oral dispersion and roller compaction are all technologies that are increasingly being used in modern pharmaceutical production and offer many advantages in terms of product quality, costs and time savings.

In essence, a granulator is a multipurpose processor that is equally suitable for the high-speed dispersion of dry powders, aqueous or solvent granulations, effervescent products, wet and melt pelletization.

At GEA we supply a complete range of granulation process equipment. With the company’s history of expertise in the market, our reliable legacy of supply, support and manufacturing excellence, you can rest assured that every pharmaceutical plant and system from GEA is a unique union of proven technology and individual solutions. Offering a wide selection of equipment, modules and systems, our experts are available to provide objective, unbiased advice on the merits and implications of each process and deliver the best solution for your specific granulation application.
Granulation Techniques

Which Granulation Process?

In the pharmaceutical industry, wet and dry granulation are most common processes employed in the production of solid dosage forms, although in certain situations, direct blending is also possible. Given the importance of granulation in the production of oral dosage forms and the technique’s extensive use in the industry, it’s essential to understand the principles and options, which are summarised below.

**Dry Granulation:** This process is used to form granules without using a liquid solution, because the product to be granulated may be sensitive to moisture (an ideal way to process compounds that are physically or chemically unstable when exposed to moisture) and heat. Forming granules without moisture involves compacting and size reduction of the mix to produce a granular, free flowing blend of uniform size.

Dry granulation can be done in two ways: either a large tablet (slug) is produced in a heavy duty tableting press or the powder is squeezed between two rollers to produce a sheet of material (roller compactor/chilsonator). When a tablet press is used for dry granulation, the powders may not possess enough natural flow to feed the product uniformly into the die cavity, resulting in varying degrees of densification. The roller compactor (granulator-compactor) uses an auger-feed system that will consistently deliver powder uniformly between two pressure rollers. When the product is compacted properly, it can then be passed through a mill and final blend before tablet compression.

**Wet Granulation:** The process of wet granulation involves the addition of a liquid solution to the powder mixture and the massing of the mix to produce granules. The fluid contains a solvent that must be evaporated, so that it can be removed by drying. Typical liquids include water, ethanol and isopropanol, either alone or in combination. Once the powders have formed into a dense mass and the granulation fluid has been evaporated then the granules are milled to an appropriate size for compression. The process can be very simple or very complex depending on the characteristics of the powders and the final dosage form. Organic solvents are used when water-sensitive drugs are processed, as an alternative to dry granulation, or when a rapid drying time is required. Because direct compression is not the best technology for many active substances, wet granulation is still a preferred method. Even if the active substance is sensitive to hydrolysis, modern equipment (a fluidized bed, for example) eliminates the problems associated with wet granulation.

Granulation 101

- Granulation is often required to improve the flow of powders or the mechanical properties of tablets.
- Granules are usually obtained by adding binders, either as solids or as liquid solutions.
- The optimal quantity of liquid needed to get a given particle size should be known to keep batch-to-batch variations to a minimum.
- Granulation is used to improve flow, compressibility, bioavailability, homogeneity, electrostatic properties and the stability of solid dosage forms.
  - Granulation involves smaller particles adhering to each other to produce larger particles or agglomerates.
- Knowledge of the powder particle size is critical to ensure consistency in the granulation process.
- Understanding and controlling the many variables in the granulation process is key to ensuring the repeatability and consistency of the finished product.
- Online sensors allow the particle size to be measured instantaneously and continuously in real-time, helping to monitor and control the granulation process.
Choosing the Right Granulation Process

GEA supplies engineering services, complete production/process plants and standalone oral solid dosage machines to customers in the pharmaceutical industry. GEA provides proven solutions for the most challenging dosage forms such as oncology drugs, multiple unit pellet system (MUPS) tablets, effervescents and multilayer pellets. Also, as experts in containment, we offer the largest variety of solutions for contained processing, based on our unrivalled experience in containment risk analysis to identify the most appropriate solution.

The following section introduces the different granulation processes, compares them objectively and presents unbiased advice on the merits of each system.

Fluid Bed Spray Granulation
Granulation can be done using fluid beds fitted with spray nozzles. Although, for many years, the top-spray position was preferred, now the advantages of tangential spray systems have become clear. The main advantage is the location of the spray nozzle, which is in an area with significantly higher shear forces that now allows the processing of formulations that could only previously be granulated in high shear processors. Additionally, the introduction of the new FlexStream™ range of fluid beds also eliminates the difficulty of scale-up. In recent years, fluid beds have improved dramatically in response to competition from single pot technology. It is now possible to contain material handling using a closed link with up- and downstream equipment. In addition, fully automatic cleaning (CIP) in fluid beds using stainless steel filters has now reached a level that compares favourably with what is possible in a single pot.

Integrated High Shear Granulation and Fluid Bed Drying
This is the most common configuration used on an industrial scale for the production of pharmaceutical granules. This system allows full integration with upstream and downstream equipment, and even includes a wet mill between the granulator and dryer. With modern control systems, it is easy to load, mix and granulate a second batch in the high shear granulator whilst drying the previous batch in the fluid bed prior to discharge. All equipment can be cleaned in place in a single automatic process.
Choosing the Right Granulation Process

**Single Pot Processing**
A mixer/granulator that dries granules in the same piece of equipment without discharging is commonly known as a single pot processor (or one-pot processor). A single pot processor is, in essence, a high shear granulator enhanced with various integrated drying options.

The basic drying principle relies on the application of a vacuum in the bowl, thus lowering the evaporation temperature of the granulation liquid. Traditionally, the heat source comes from the heated dryer walls, and the heat transfer rate is related to the surface area of these walls and the volume of product being processed. As such, this direct heating method is most effective for small-scale applications or those using organic solvents or low quantities of binder fluids.

Introducing stripping gas into the pot allows very low final moisture levels to be achieved (only required in particular applications). A small quantity of gas is introduced at the bottom of the equipment, which passes through the product bed, improving the efficiency of vapour removal. However, as the heated wall is the only source of drying energy, the same limitations exist as for ‘pure’ vacuum drying.

Microwave energy can be used to overcome these limitations. This provides a further source of energy that also enables the efficient drying of larger quantities of binder fluids and water-based granulations. With organic solvents, vacuum and microwave drying provide an additional advantage regarding exhaust gas treatment; only pure organic vapours need to be dealt with, as opposed to a mixture of solvent and large volumes of process gas, which would be required with most other wet granulation technologies.

**Fluidized Spray Drying (FSD)**
FSD produces granules from a liquid in a one-step process. One option is to produce the active in the primary production step as granules, so that it only requires blending with excipients suitable for direct compression for secondary processing. This can only be done with actives that are tacky (in a wet state); otherwise, the addition of a binder is necessary. Another possible use of FSD technology is to mix all the ingredients into a solution or suspension and to produce granules in a one-step operation.

During the FSD process, the liquid feed is atomised at the top of the tower in a concurrent mode. After the liquid is evaporated, the subsequently formed particles leave the drying chamber together with the exhaust air. These particles are then separated in a cyclone or filter and reintroduced into the drying chamber where they come into contact with wet droplets and form agglomerates. After these agglomerates have reached a certain weight, they cannot leave via the top of the tower with the exhaust air, but fall down into the integrated fluid bed at the bottom of the drying chamber. Here they are dried and cooled before being discharged.

However, this type of equipment is difficult to clean, particularly the external pipe work, when changing to another product. Systems have, therefore, been developed in which the external pipe work does not come into contact with the product.

**Melt Granulation:** In a melt granulation process, the binder solution of a standard wet granulation process is replaced with a meltable binder. This binder can be added in molten form, but the high shear process offers the benefit of allowing the binder to be added in its solid state. Melting is achieved by the energy provided by friction in the mixer and the heated jacket of the bowl.

**Effervescent Products:** A very small amount of water is added to start the pre-effervescent reaction: some of the carbon dioxide is released during granulation, but water is also produced as a reaction product; this then acts as a granulation fluid producing more carbon dioxide and also more water. This avalanche needs to be stopped at a certain point by starting the drying process and removing the water. This can be done using a high shear granulator with subsequent fluid drying by discharging the material at the end of the granulation process into a pre-heated fluid bed dryer or a single pot processor.
Continuous Granulation
As a result of various regulatory initiatives to improve product quality and to reduce the risk of product failure, there is a huge interest in continuous processing. A typical system has three modules: a wet high shear granulation module, a segmented dryer module and a granule-conditioning module. In the granulation module, dry ingredients are dosed individually or premixed into the continuous high shear granulator. After a small dry mix section, the granulation liquid is added, so each particle receives the same amount of liquid. The whole wet granulation process takes place in a few seconds with only a few grams of product in process at a given time, resulting in faster start-up and minimal losses. The particle size can be adjusted by changing the working level in the granulator; this results in a continuous flow of wet granules with a constant quality and density that is transferred to the dryer. There are no oversized agglomerates and thus no wet milling.

The dryer module, based on the fluid bed drying principle, splits the continuous flow of granules in small packages, drying them each in a separate segment of the dryer. When the content of a segment has reached the desired moisture level, it is emptied and transferred to the granule-conditioning module and refilled with a new package of wet granules. The drying curve of each package is monitored. In the granule-conditioning module, the dried granules can be measured for critical quality attributes such as particle size distribution, humidity and content uniformity. At any time, there is only a few kg in process, which minimises the amount of at-risk product. The unit’s small size and modular construction allows for fast deployment, simple scale-up and makes it easy to install within existing buildings.

Beyond the Granulator
For full compliance with national, local and in-house regulations, GEA offers a range of emission control options, including solvent recovery systems, outlet filters and full containment plants. Equipment can be supplied to meet explosion-proof and pressure shock standards as required. Our high shear granulator plants and granulation and drying process expertise is based on a wealth of experience and a long history of research and development. With plants installed around the world and, quite literally, thousands of tests performed, we have established a solid base of expertise related to the needs of the pharmaceutical manufacturing industry. We have the right solution for your granulation application.
GEA has supplied shear granulator plants and granulation and drying process expertise to various industries for more than a century, and to the pharmaceutical industry in particular for more than 50 years. This includes small capacity systems designed for R&D as well as industrial size plants for the batch and continuous production of pharmaceutical compounds under cGMP conditions.

With both top and bottom drive granulators available, we can help you to select the technology that is most suitable for your product and process.

The GEA high shear mixer and granulators — PMA™ and UltimaGral™ — are multipurpose processors that are equally suitable for the high speed dispersion of dry powders, aqueous or solvent granulations, effervescent products and melt pelletization. The design of both the Gral™ and the PMA™ allows for different ways to set up a standalone machine in a GMP-compliant manner. And, whether your installation is standalone or fully integrated, several features are available to ensure completely contained processing, such as GEA high containment split butterfly valves, isolator boxes and vacuum transfer systems. Contained processing also requires that the equipment can be cleaned in a contained fashion. Our high shear granulators can be equipped with a full CIP system that ensures cleaning-in-place of the product feed, product filter, bowl, lid and discharge valve. Even downstream equipment such as a mill can be incorporated in the CIP system.

Having established a credible pedigree of expert know-how in the pharmaceutical manufacturing industry, GEA provides optimal solutions for your applications: no other supplier offers such a complete range of granulation and drying equipment.
PMA™ High Shear Mixer Granulators
The PMA™ family — PMA™ classic, PMA-Advanced™ and PharmaConnect™ — provides total flexibility in system design and capacities of 1–1800 L. It is the ultimate in versatility, with modular options for blending, high shear granulating and wet pelleting. The design maximises product processing and handling containment. User-selected standard process modules are combined with advanced automation and cleaning-in-place (CIP) systems to create custom solutions that meet individual needs.

Key features include the following:
• process containment
• complete ease of operation (fully automated or manual)
• advanced process control for repeatability
• latest end-point detection techniques
• full opening cover for easy inspection
• modular upgrades are available for future requirements
• integrated WIP or CIP
• available as standalone or through-the-wall installations
• impeller and chopper options.

PMA™ Production capacities

<table>
<thead>
<tr>
<th>PMA size</th>
<th>150</th>
<th>300</th>
<th>400</th>
<th>600</th>
<th>800</th>
<th>1200</th>
<th>1800</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical Weight@0.6 g/mL kg</td>
<td>60</td>
<td>120</td>
<td>120</td>
<td>240</td>
<td>320</td>
<td>480</td>
<td>720</td>
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Impeller and Chopper Options

Tapered Blade Impeller:
The standard impeller, designed for use with the conical bowl of the PMA™ high shear granulator.

M8 impeller:
An innovative swept-back design for improved mixing characteristics, faster processing and a more clearly defined end-point.

U-Shaped chopper:
The standard chopper, typically paired with a tapered blade impeller, to assist with the dispersion of granulation fluid throughout the batch.

Fir-tree chopper:
A multi-blade design improves binder solution dispersion and product movement at slow speeds.
High Shear Granulation
Top Drive

UltmaGral™

UltmaGral™ High-Shear Mixer Granulators
With the Gral™ range, GEA pioneered the market for top-driven high shear mixer granulators. Still in demand after numerous product upgrades, this state-of-the-art processing workhorse is available with a wide range of bowl capacities to suit any production requirement. The equipment is built to comply with current cGMP standards and is recognised by companies worldwide as being low maintenance, high quality, robust and reliable.

Designed for production-scale functionality, special mixing tools are available for specific applications, as well as a jacketed bowl for temperature control during the process. And, as bowl shape, mixing tools and process parameters are exactly the same, all processes running on the Gral™ range can be immediately transferred to the UltmaGral™ and single pot UltmaPro™ granulators without changing any parameters.

With bowl capacities of 10–1200 L (useful bowl content up to 2/3 of gross capacity), the UltmaGral™ range can cover all requirements after the formulation stage. From clinical batch production for scale-up trials to large-scale production for marketed products, scalability is key to the system’s success. The most important features of this design are the top-driven mixer and chopper, the removable bowl (Gral™ range only) and the through-the-wall installation of the larger machines.

Additional features include the following:

• easy to Wash-in-Place (WIP)
• built to GMP-standards
• total containment of the product
• ANBA™ mixer arm
• variable speed chopper and impeller
• operator control panel on the machine
• automation/PC/PLC controls
• controlled product discharge
• automatic end-point detection with PROCOLL-software
• explosion proof design
• heating and cooling units
• Fill-O-Matic (vacuum) or gravity loading system.

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<th>Production capacities</th>
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<tr>
<td><strong>GRAL size (L)</strong></td>
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<tr>
<td><strong>Bowl Volume</strong> (L)</td>
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<tr>
<td></td>
</tr>
<tr>
<td><strong>Typical Weight @ 0.6 g/mL</strong> (kg)</td>
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PharmaConnect™ R&D High Shear Granulation
This innovative system provides a unique benefit to the pharmaceutical development industry, integrating a single control unit with a diverse range of process modules. Based upon GEA’s class-leading PMA™ and Gral™ granulation technologies, the PharmaConnect™ provides the user with the ability to process batches from as little as 100 g, right up to 25 kg or more, all from a single control system. Standard module capacities are set at 1, 3, 5, 10, 15, 20, 30 and 60 L (with each unit being geometrically scalable). Critically, each of these modules features its own impeller drive motor, maintaining a consistent energy input per unit volume. By providing this level of flexibility, the development scientist operating at the 1 L level can provide true scale-up data for commercial expansion.

However the PharmaConnect™ is not limited to just granulation; the unique design of the control unit allows any number of process technologies to be operated from the single operator interface. The key technologies offered include high shear granulation, extrusion and spheronization, IBC blending systems and high shear blending.

<table>
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<tr>
<th>PMA size</th>
<th>1</th>
<th>3</th>
<th>5</th>
<th>10</th>
<th>15</th>
<th>20</th>
<th>30</th>
<th>60</th>
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<tbody>
<tr>
<td>Operating Range Litres</td>
<td>0.4–0.75</td>
<td>1.2–2.25</td>
<td>2.0–3.75</td>
<td>4–7.5</td>
<td>6–11.25</td>
<td>8–15</td>
<td>12–22.5</td>
<td>24–45</td>
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<tr>
<td>Typical Weight® kg</td>
<td>0.4</td>
<td>1.2</td>
<td>2.0</td>
<td>4.0</td>
<td>6.0</td>
<td>8.0</td>
<td>12.0</td>
<td>24.0</td>
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Using proven standard components, GEA makes plant design both simple and flexible. User-selected process modules, filters, control systems and air preparation units can be combined in a system that meets your process requirements exactly. This modular approach ensures that qualification and validation procedures are kept to a minimum.

Process Technologies
For maximum process flexibility, GEA can supply a single fluid bed unit or the patented FlexStream™ fluid bed processor that combines multiple processes in a single process container. GEA has a series of fluid bed processors that are suitable for formulation, process development, the production of clinical material through to full-scale production; the philosophy behind the design is that a combination of standardised modules can be built together to meet specific requirements. As such, dryers of equal capacity may be completely different with respect to design, configuration and physical size.

FlexStream™ Fluid Bed Processor
Fluid bed operations such as drying, granulation or particle coating are often major process steps in the production of solid dosage forms. And, even though fluid beds have been in use by pharmaceutical companies for more than 50 years, GEA continues to enhance the design, introducing new technologies to optimise performance and improve process understanding. In the past, the individual fluid bed processes have required dedicated equipment to achieve the optimum performance, leading to additional capital expense. Furthermore, the scale-up of fluid bed processes has never been addressed.

From a performance standpoint, granules produced by fluid bed granulation often show excellent compression behaviour but can be weak and flow poorly (compared with high shear granulation). Some formulations can’t be granulated in a fluid bed at all, and coating applications based on conventional Wurster columns are subject to a number of drawbacks, such as scale-up issues, loss of coating material and agglomeration losses.

Using proven GEA fluid bed technology to achieve fluid bed granulation, drying and pellet coating (or tablet coating) in a single module, FlexStream™ is a new multipurpose processor that addresses the current shortfalls of traditional fluid bed processing, including linear scale-up, fully contained loading and unloading, and superior product homogeneity for both LOD and PSD. Requiring only one product container for all unit operations, the FlexStream™ reduces your build envelope (both height and footprint) and provides PAT-compatible inline particle growth measurement.

The FlexStream™ concept has the additional advantage that no mechanical adjustment is necessary to switch between using the equipment as a dryer, a granulator or a coater. And, impressive test data prove that, in addition to these commercial benefits, FlexStream™ gives superior product quality when compared with conventional top-spray granulation or Wurster coating.
Current Good Manufacturing Practices increasingly require that product is fully contained during processing to protect operators and the environment. Integrated process systems not only offer containment but also improved productivity through automation, increased yield and efficient cleaning procedures.

Key features include the following:

- **WIP and CIP:** Process optimisation depends on efficient, effective cleaning. Automation of the cleaning process ensures repeatability, allows validation and minimises downtime.

- **Rapid discharge using lean phase conveying system:** Enhanced by the Non-Sifting Gill Plate™ airflow from both above and below, the air distributor is used to discharge the dry granules in a very efficient manner, avoiding the need to place the receiving container under negative pressure.

- **Through-the-wall installation:** Ensuring that all auxiliary equipment is housed outside the process room, this greatly simplifies GMP compliance.

- **Solvent emission control:** A range of open- and closed-cycle systems to remove or recover organic solvents is available.

- **Spraying systems:** Nozzles, pumps and liquid preparation units are supplied according to process needs.

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<th>Production capacities</th>
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<tr>
<td><strong>Flexstream™ size</strong></td>
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<tr>
<td><strong>Typical Batch Weight (@0.5 g/mL) kg</strong></td>
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</table>
MP-1

For true process flexibility and as an introduction to production-scale processing, the MP-1 is the machine of choice. Capable of performing any fluid bed process, the MP-1 features a diverse range of options, including high efficiency drying, top-spray granulation, bottom-spray pellet coating (Precision Coater™) and side-spray granulation/coating (FlexStream™). With a batch range from 250–6000 g, the MP-1 complements the GEA family of granulation and pelletization equipment, but still maintains the flexibility offered by a modular, mobile design.

STREA-1™

And, combining versatility with benchtop practicality, the STREA-1™ is the flexible choice when taking the first steps towards process optimisation (drying, top-spray granulating and coating) in 200–2000 mL volumes, thanks to its interchangeable components and containers.
Fluid Bed Processing

Process filters
In granulation, drying, and most pelletizing applications, a process filter is used to trap small particles, which are returned to the bed when the filter is cleaned. In coating applications, fine particles usually need to be removed. Fluid beds that are used for more than one type of process can be supplied with interchangeable process filters.

Single shaker bag filter
A simple, basic filter with a single bag, which is cleaned by shaking. Fluidization stops during filter cleaning.

Multi-shaker bag filter
This filter is divided into two or more sections, with a separate filter bag in each one. Bags are cleaned individually by shaking the filter, while fluidization continues in the other sections, for faster and more efficient production.

Blow-back filter
There are multiple filter bag sections in this design. Cleaning takes place one bag at a time, so that a large proportion of the filter is always available for continuous fluidization.

Cartridge filter
Stainless steel filter cartridges are cleaned one at a time, so that a large proportion of the filter is always available for continuous fluidization. Unlike bag filters, this system can be cleaned-in-place.

Particle retainer
Used for coating applications, this design retains the coarser particles and returns them to the process, removing the dust to an external filter unit.

Integration
Fluid bed dryers and coaters can be combined with top-drive and bottom-drive high shear mixer-granulators, wet and dry milling facilities, product handling systems, binder and coating preparation units and filtration units, all designed for fully integrated systems. Safety, containment, product flow and building requirements are in-built for full integration and optimum process efficiency.
The GEA UltimaPro™ single pot (or one pot) technology offers a choice of mixing, granulating and drying options that are integrated into a single processing vessel. With our help, this allows the customer to choose the most appropriate technique for the product.

With high shear granulation technology at its core, single pot processing relies on the application of a vacuum within the bowl to dry the wet mass. This technique allows pharmaceutical compounds to be dried at very low temperatures and, even if organic solvents are used during the granulation process, an efficient solvent recovery systems means that environmental exhaust levels are minimal.

**Single Pot technology**

Single pot processing is an extremely flexible technology; with its various processing options, it’s ideal for many different applications and products. Whether for standard wet granulation, melt granulation, pelletizing or effervescent production, and combined with vacuum or microwave drying, a single pot processor can achieve the required result. The swinging bowl option enhances this flexibility even further by being able to process older formulations to a high quality standard. Quick product changeover is simple and efficient, and the equipment is easy to clean as a result of the clean-in-place (CIP) system.

As the overall investment cost for a technology — including installation and the required current Good Manufacturing Practice (cGMP) space — is becoming more and more important in the pharmaceutical industry, minimising equipment footprint is a key concern. Single pot processing is a very compact technology, achieved by incorporating several manufacturing steps into one machine. This reduces the capital cost of the equipment and, by reducing the cGMP and technical space required for granule production, the overall project cost.

In addition, because of its very nature, a single pot process is contained. No transfers are required between process steps, except to load the raw materials and unload the dry granules. This is not only beneficial for the operators, protecting them from potent products, but also to protect the products from external influences such as heat, light or moisture. Specific solutions are available for product loading and discharging that achieve the desired level of containment for the whole process.

For process control and monitoring, a range of control systems is available that offer maximum flexibility and functionality for process visualisation, automation and data recording. And, by combining process monitoring using online, PAT-compatible analysers with solid process engineering principles and advanced process modelling techniques, we enable processes to be actively controlled to compensate for minor input variations (such as raw materials), so that the specifications for the final product will be closer to the ideal target.
UltimaPro™ Single Pot Processor

With capacities from 10–1200 L, the UltimaPro™ range can cover all your requirements, starting with the process development stage and clinical batch production to scale-up trials and large-scale production for marketed products.

The through-the-wall configuration offers the best option in terms of cleanliness, maintenance and explosion protection, providing a sealed division between technical and GMP space that offers containment, explosion area separation and compliance with requirements such as ATEX. By keeping technical components out of the process room, the equipment is much easier to clean. Maintenance is done in the technical area, removing the need for the operator to work in a GMP environment and reducing both downtime and the risk of contamination.

The UltimaPro™ can be equipped with a ‘moveable head’ to enhance flexibility. This feature allows operators to lower the closed bowl to enable better accessibility and easy loading. The closed bowl can also be raised for dust-free discharging. This option is extremely useful in height-constrained processing areas.

Swinging bowl: The use of the swinging bowl during vacuum drying results in improved granule characteristics and a reduction in drying time. It is a very gentle method that agitates the product during drying, producing fewer fines and, as such, allows the processing of formulations that were not explicitly developed for vacuum drying in a single pot processor.

Drying Options

After wet granulation, the granulation liquid needs to be eliminated to achieve stable, dry granules that can be further processed. The UltimaPro™'s vacuum system has been designed to yield optimal drying efficiency. Incorporating condenser systems and selecting the right pumps can achieve excellent solvent recovery and a competitive drying rate. Different configurations are available to suit any process requirements.

Gas-assisted vacuum drying (Transflo™): The vacuum drying process can be enhanced by the addition of a small amount of gas that passes through the product during the drying phase. Designed for optimal distribution of the stripping gas through the product, the Transflo™ technique results in shorter drying times and a lower residual moisture content of the final product without compromising on inspection, validation or cleanability.

Microwave drying: To really enhance the drying process, microwaves can be added as an additional energy source. By carefully controlling the product temperature and directing the reflected microwave power, this technique is ideal for the rapid processing of pharmaceutical products. Undoubtedly the fastest single pot drying method available, our system is equipped with control and safety features that ensure excellent process control and complete safety for product, operator and equipment.

Production capacities

<table>
<thead>
<tr>
<th>UltimaPro™ size (L)</th>
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<th>25</th>
<th>75</th>
<th>150</th>
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<th>400</th>
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<tr>
<td>Bowl Volume (Litres)</td>
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<td>303</td>
<td>400</td>
<td>614</td>
<td>900</td>
<td>1166</td>
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<tr>
<td>Typical Weight@ 0.6 g/mL</td>
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<td>11</td>
<td>30</td>
<td>60</td>
<td>120</td>
<td>160</td>
<td>240</td>
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Single Pot Processing

Special Applications

**UltimaPro™-HC**: Containment tools for loading and discharging (Hicoflex®, MC valves, etc.), a fully validated CIP system, PAT-compatible sampling options for end-point determination and a HEPA filter-based vacuum system are all supplied as standard. The basic vacuum drying technology can be enhanced with microwaves to increase yields by optimising process parameters and reducing the amount of wet lumps and sticking.

**UltimaPro™-Eco**: Equipped with a highly efficient vacuum system that facilitates the recovery of solvent vapours (up to 99.5%), optional police condensers or active carbon filters can also be integrated to eliminate all solvent emissions. The whole system is designed and certified to comply with ATEX guidelines. The basic vacuum drying technology can be enhanced with microwaves to improve processing times. Benefits include easy and low-cost solvent recovery by condensation, waste reduction, safe solvent processing using vacuum drying, explosion protection (nitrogen inertisation), PAT integration and fast, flexible processing.

**UltimaPro™-FZ**: Equipped with a highly efficient vacuum system and a specially balanced design for water-based effervescents, the bowl is leak-tight to enable a vacuum level of <3 mbar to be achieved. Standard effervescence formulation recipes can be integrated into the system. The basic vacuum drying technology can be enhanced with microwaves to reduce processing times, improve yields and deliver a more stable end-product. The flexibility of single pot processing makes it suitable for all effervescence production methods (single- or multi-step, solvent- or water-based).
Case Study: Ranbaxy Laboratories Ltd

Using proven standard components, GEA can supply both simplicity and flexibility in plant design. User-selected process options, control systems and liquid recovery units combine in a system that meets your process requirements exactly. This approach ensures that qualification and validation work can be kept to a minimum and ensures successful results. As demonstrated in this case study, for example, we have a leading position and a proven track record as a system integrator for high containment projects with single pot technology for oncology and hormone applications.

Top-End Containment Line for Anticancer Drugs

GEA supplied a complete containment line to Ranbaxy Laboratories Limited (Gurgaon, India) to manufacture highly potent anticancer drugs with an OEL of 1–10 µg/m³. It was essential that the process prevented any cross-contamination in the production area and limited operator Real Daily Intake (RDI) of hazardous substances to well within the Acceptable Daily Intake (ADI).

During the selection process, several key equipment features were specified:

- all units had to provide full containment
- the entire process had to be contained in a single machine to avoid contamination and limit material handling
- the technology had to be flexible enough to adapt to different products and batch sizes
- the process should provide maximum yields with minimum wastage
- there should be a clear and straightforward documentation procedure.

In addition, it was essential that the operators had an in-depth understanding of both the equipment and the relevant containment issues.

To meet the production, containment and whole-life cost requirements, Ranbaxy chose two single pot processors from GEA: the UltimaPro™ 10 and the UltimaPro™ 75 (10 L and 75 L processing bowl, respectively). The safe, low temperature, vacuum drying technology was augmented with microwaves or Transflo™ (gas-assisted vacuum drying); end-point determination was achieved using a torque sensor (granulation) and NIR (end humidity); a built-in camera allowed operators to view the process without opening the lid; and cleaning was done by a comprehensive fully validatable CIP system.

The new equipment has allowed the company to develop niche oncology products in a contained environment that protects its workforce and the wider environment from toxic compounds. Since installation, predicted levels of production, containment and operational efficiency have been achieved. In addition, factors such as very effective microwave drying for aqueous feeds, more consistent granule sizes and much less operator intervention than had been anticipated have been cited as “areas of exceptional performance.”

Lalit Sood, Projects Director for Ranbaxy, said:

“The unit cost reduction has opened up the market and enabled the company to provide a hard-to-resist proposition worldwide. The GEA technology gives us security of outcome with the guaranteed quality and consistency we need.”
Continuous Granulation

ConsiGma™ 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 put in place by the regulatory authorities.

The ConsiGma™ system is designed for plug flow, first-in first-out production, avoiding back mixing, providing consistent quality and allowing for the inline control of critical quality attributes. It consists of three modules: a wet high shear granulation module, a segmented dryer module and an evaluation module.

Powder supply: Up to four different feeders can be installed on the ConsiGma™ high shear in-line blender, dosing is done by loss-in-weight feeders and a low shear inline blender can (optionally) be integrated.

High shear mixing and granulation: The twin screw granulator is based on the plug flow principle, accurate liquid dosing enables inline torque control, there’s no risk of pressure build up and a second liquid dosing is available when the binder is dissolved in liquid.

ConsiGma™ segmented fluid bed dryer: The dryer module, based on the fluid bed drying principle, splits the continuous flow of granules in small packages, drying them each in a separate segment of the dryer. The drying curve of each package is monitored, and either time- or temperature-based discharges are possible.

Granule conditioning unit: Granule calibration, online analysis (control – reject – stop) and inline external phase and lubricant blending come as standard.

Tableting: The MODUL™ P rotary tablet press offers equal final compression forces for all tablets and adjustable dwell times at pre- and final compression; a continuous coater can also be integrated.
ConsiGma™-25
The ConsiGma™-25 can handle flexible batch sizes from 500 g up to several tons. There is no process scale-up as time is the only relevant factor in a continuous process, which dramatically reduces development time and costs. The system is compact (one third that of a classic granulation line), modular — so fits perfectly into any R&D department or existing solid dosage suite (inclusive of a tablet press) — and subscribes to the philosophy of Quality by Design (QbD).

Typical applications for ConsiGma™ include producing small batches of high added value products, the production/launch of new molecules, reformulations and current non-robust processes, formulations with specific granulation and/or drying issues, site changes or increases in production and more economic and greener production methods. ConsiGma™ offers you
• maximal end-product safety using online quality control
• 10 times faster testing in R&D
• 40% saving on labour
• reduction of manufacturing space by 60% compared with current standards
• 50% energy savings based on reduced power and heat recovery
• from 0.5–5% yield improvement.

With its light weight, ultra small size and modular construction, ConsiGma™ fits perfectly in every R&D department or an existing tablet production room. No need to change the building, just wheel it in, connect the power and an air supply and off you go. Installation time and cost are reduced to a fraction of the current benchmark.

ConsiGma™-1
The ConsiGma™-1, designed for fast and easy deployment in R&D labs, is capable of running batches of a few hundred grams up to 5 kg or more, with less than 10 g of product held up in the process and product losses of less than 80 g. Because of the fast processing times, minimal retention times and flexibility of the system, it is ideal for developing your formula and process parameters using DoE. The process parameters developed with ConsiGma™-1 can be directly transferred to the full-scale ConsiGma™ system.
The Six Benefits of ConsiGma™ Continuous Processing

Plug flow: FiFo concept for each process step
- Proven and guaranteed by PEPT and powder tracing
- Full and comprehensive product tracing
- Real-time monitoring and process control
- Improved and guaranteed end-product quality.

System and control integration
- Seamless integration between all process units and peripheral equipment
- No need for intermediate storage in bins or expensive product transfer
- PAT tools for inline measuring and control of QCAs: BU, CU, LOD and PSD
- Reduced GMP area, fewer QC activities/batch and simplified logistics.

Modular approach and built-in versatility
- All modules fit through standard pharma doors
- Smooth integration of different OSD processes with ConsiGma™
- Melt granulation, direct compression, roller compaction
- Multiple-use process line and fast deployment.

No scale-up and limited amount of active used for product transfer
- From ConsiGma™-1 (R&D) to ConsiGma™-25 (clinical study, product launch and production)
- No scale-up for granulation and drying process
- Direct transfer of recipes and process parameters
- Each single DoE test involves approx. 1 kg of product (production)
- Avoid intensive and expensive scale-up activities and corresponding troubleshooting.

Process highly potent drugs
- High containment execution with split valves and liner technology
- Wash-in-Place concept for maximum operator safety
- Reduced filter surface and product contact area for increased yield
- Single-room operation to avoid cross-contamination.

Upgrade from bin-to-bin to continuous with RTR
- Modular integration of continuous tablet and coating suite
- PAT tools, process monitoring and control
- Be ready for the future!
Current good manufacturing practices increasingly require that product is fully contained during processing to protect both operators and the environment. Integrated process systems not only offer containment, but also provide improved productivity through automation, increased yield and efficient cleaning procedures. Furthermore today’s increased demands for customised design, special construction materials, surface treatments, advanced control systems, compliant production and process validation have resulted in continuous improvements in solid dosage plant design for the pharmaceutical industry.

Integration by Design
GEA is uniquely qualified to provide integrated pharmaceutical process lines. Drawing on its world-class expertise and technologies, we offer an entire range of state-of-the-art process equipment that has been designed and built with system integration in mind. A modular approach allows customers to select standard process modules to suit project needs: fully integrated turnkey installations can be supplied, including fluid bed process equipment combined with top- and bottom-drive high shear mixer-granulators — from GEA — with integrated contained materials handling, wet and dry milling facilities, product handling systems, binder and coating preparation units, filtration units and GEA tablet compression.

Our distinctive specialisation lies in the integration of GEA containment technology into complete solutions for pharmaceutical solid dosage form facilities. With an emphasis on quality and GMP standards, we are committed to working together with our customers to deliver custom-built, first class solutions for projects of all sizes and complexity.

Safety, containment, product flow and building requirements are in-built for full integration and optimum process efficiency. Our service includes design, installation assistance, commissioning and process validation, as well as training and technical support. IQ, OQ and all other documentation comply with FDA/GAMP guidelines.

PAT
The FDA’s PAT (Process Analytical Technology) initiative has enabled GEA to combine its equipment design skills and process engineering know-how to integrate online (PAT) analysers into its systems in a way that can provide real insight into the operation of the process and help customers to achieve key product quality targets. The goal of the PAT initiative is to ensure that pharmaceutical products are manufactured using processes that are understood and monitored so that the key quality characteristics of the products can be actively controlled.

Combining process monitoring with solid process engineering principles and advanced process modelling techniques will enable procedures to be actively controlled to compensate for minor input variations (raw materials), so that the specifications for the final product will be closer to ideal targets. Built into the control system, GEA has integrated its process knowledge to help operators monitor and control their processes. For several process steps, end-points based on process parameters are available, and guidelines are given depending on the set points entered. In addition, GEA has experience with integrating innovative analytical tools for process monitoring and control.
Cleaning and Maintenance
Process optimisation depends on efficient, effective cleaning. Automation of the cleaning process ensures repeatability, allows validation and minimises downtime. In recognition of the fundamental role played in today’s advanced powder processing industry by automated clean-in-place procedures, GEA has developed a unique approach to CIP.

Concealed services: The integrated design ensures that all lines and hoses for the utilities of the plant (water, electricity, hydraulics, etc.) are concealed. This creates a safe and uncluttered working space.

CIP and WIP systems: More efficient cleaning is one of the key advantages of system integration. We provide validated cleaning with minimal downtime. GEA offers CIP-by-design features in all of its processes. Every aspect of the integrated plant, from inlet to discharge, has been value-engineered for optimum cleanability. Spray system, tanks cleaners, nozzles and seals are an integral part of our equipment design.

Safety and the Environment
For full compliance with national, local and in-house regulations, GEA offers a range of emission control options including solvent recovery systems, outlet filters and full containment plants. Equipment can be supplied to meet explosion-proof and pressure shock standards as required.

Extensive safety testing confirms pressure enhancement effects and identifies safe design limits for integrated systems. GEA, in conjunction with the FSA, the safety specialist centre in Germany, has completed an extensive test programme involving more than 100 test explosions. This research has shown conclusively that should an explosion occur during the transfer operation in an integrated system in which a granulator is connected directly to a fluid bed dryer without an explosion isolation valve, the secondary explosion pressure in the granulator can be significantly higher than in the fluid bed. These tests have enabled GEA to gain full EC type approval for a range of pressure shock resistant integrated systems and 16-bar pressure shock resistant high shear granulators.

Lighthouse Probe™ Technology
GEA has joined forces with J&M GmbH to create a compact and cleanable in-process optical probe for use in powder processing equipment.

The novel Lighthouse Probe™ can be used with a range of spectroscopic techniques, including NIR and UV/Vis, to overcome the traditional problem of product sticking to the observation window. The probe is compact and easy to install and makes it possible to take a reliable in-process measurement of quality critical product characteristics including:
- material and active content identification
- active content uniformity during high shear blending operations
- moisture content and end-point during drying processes
- coat growth during coating processes.

Optical methods such as UV/Vis or NIR spectroscopy can be very powerful tools for analysing a range of product characteristics, but in processes involving wet and sticky powders it is necessary to ensure that the system has a clear view of the product. Conventional windows used in process equipment such as fluid bed systems or high shear granulators have always suffered from the risk of window fouling. The GEA and J&M Lighthouse Probe™ has overcome this problem.
GEA specialises in contained materials handling solutions for primary and secondary pharmaceutical and healthcare companies. With GEA high containment split butterfly valves, we offer a wide range of technologies and equipment that improve and enhance the efficiency and performance of solid dosage form plants for the safe transfer of powders.

**Containment and Granulation**

Designed for integrated containment, GEA specialises in the design and manufacture of fluid bed and high-shear granulation technology and is uniquely qualified to provide integrated, state-of-the-art high sheen mixer-granulator and fluid bed drying solutions. A modular approach means that customers can select standard process modules to suit their project needs.

Fluid bed dryers and coaters can be combined with high sheen mixer-granulators, wet and dry milling facilities, product handling systems, binder and coating preparation units, and filtration units, all of which have been designed for use in fully contained integrated systems. Safety, product flow and building requirements are built in for full integration and optimal process efficiency. Key technologies and products include containment valves, Hicoflex® and docking systems for safe powder handling, single or multi-level configurations, powder discharge solutions (Vibrollow®), CIP, inline milling, vacuum transfer and contained charge vessels.

**Single pot processing:** By definition, a single pot process is contained, making it the first choice for the granulation of highly potent compounds. No transfers are required between process steps, except to load the raw materials and unload the dry granules. This not only protects the operators from exposure to potent products, it also protects the products from external factors such as heat, light and moisture. Specific solutions are available for product loading and discharging to achieve the desired level of containment for the whole process.

**System integration:** Our distinctive specialisation lies in the integration of GEA containment technology into complete solutions for pharmaceutical solid dosage form facilities. With an emphasis on quality and GMP standards, we are committed to working together with our customers to deliver first-class, tailored solutions for projects of all sizes and complexity. With worldwide references, GEA has developed an outstanding reputation for quality and service to become the clear leader in contained materials handling technology.
Feeding the Granulation Process
The effective and safe transfer of both excipients and active ingredients is essential. A number of options are available:

Gravity feeding: Gravity loading through a discharge station from above or via a post hoist are ideal solutions for guaranteed containment and easy cleaning. API discharge vessels can be used to deliver more potent formulations directly into the granulator.

Vacuum feeding: When room height is a limiting factor, a contained vacuum station can be used: incorporating containment valves that improve airborne dust levels, they can help to reduce area classification categories. Interlocking containment valves with a nitrogen purge system can also be used.

Unloading granulation equipment: Inline sieving or milling can facilitate the granule loading process. A lubricant or other materials can then be added (often done using charge containers or Hicoflex® bags) and blended with the granules.

Risk Assessment
Even for experienced manufacturers, 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, it also boasts unrivalled 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, optimising 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.

Contact us today to learn more about our extensive containment experience and discuss your specific project.

We have the right solution for you.

Case Study: Penn Pharma
After conducting extensive market research, Penn Pharma identified an increased need in the solid dose oncology market for the outsourced development and production of highly toxic drugs. Its production site had been manufacturing potent solid dosage products for more than 20 years but needed additional capacity.

Penn Pharma elected to work with GEA because of its proven track record in containment technology and expertise in creating fully integrated production lines. GEA’s approach was to eliminate the use of isolation suits in favour of containment interfaces (BUCK® MC high-containment valves and Hicoflex®).

The new plant now includes the first commercial PharmaConnect™ “through the wall” system in Europe. The contained R&D line for wet granulation also includes the dispensing of excipients and potent powders, GEA’s PMA™ 150 and FlexStream™ 1000 for granulation and drying, dry milling, granule collection and blending, tablet compression using a MODUL™ P tablet press with a Wash-off-Line ECM (exchangeable compression module) and pellet coating.

The plant also has a contained R&D line for direct compression and a separate production line that offers containment interfaces for powders, API and excipient dispensing, dry milling and powder collection and blending. Penn Pharma is now a single source for the development and production of highly toxic drugs at one of the world’s most advanced and efficient plants. The project has significantly increased their capacity and the company can now manufacture approximately 500 additional batches during a standard two-shift operation.
Based on our strong commitment to research and development, pharmaceutical technology centres in Belgium, Denmark, Switzerland, the UK, the USA, Singapore, China and South Korea provide global technical support and know-how to the pharmaceutical industry.

These centres of excellence give you access to a full range of test facilities and teams of experts, all of whom work closely with our customers to optimise processes and evaluate their products, enabling them to achieve their process and production goals.

At our technology centres, you, the customer, can test any unit operation, from lab to pilot scale: you can perform comparative process studies with our skilled operators by testing complete process trains, where all processing is optimised by utilising advanced PAT and CIP technology.

In addition, you can rely on a permanent staff of experienced engineers, technicians and industrial pharmacists who can assist you with any production problems, new developments and the adaptation of GEA technology to your needs.

Our staff remain constantly up to date with the most recent developments in the industry to be able to provide you with the best assistance possible.

**Europe**

**Solid dosage process test centre**: Located in Bubendorf, Switzerland, we help pharmaceutical companies bring new products to market quickly, effectively and with easy scale-up to full production; the centre is equipped with a full range of solid dosage processes, including contained material handling, dispensing, blending and powder mixing, granulation, extrusion, pelletization, drying, tablet compression (with built-in PAT) and coating.

**Pharma continuous tableting**: Build quality into your process, make inline PAT measurements and optimise your process to drive the critical quality attributes to the requested target levels; situated near Antwerp, Belgium, a permanent staff of experienced engineers, technicians and industrial pharmacists can demonstrate the ConsiGma™ technology and explain why the pharmaceutical industry is looking towards continuous processing to improve their production quality in the most efficient way to the level requested by the authorities today.

**Single pot processing**: The Process Development Centre, near Antwerp, Belgium, offers expertise and advice on new product trials, feasibility trials, scale-up studies, process support at customer sites and training programmes; this service greatly benefits both the industry’s R&D and manufacturing groups as the production and process engineers are involved in the selection of equipment and process optimisation. All processing is optimised by utilising advanced PAT and CIP technology.

**Spray drying process development and contract manufacturing facility**: Located in Copenhagen, Denmark, this is the largest and most advanced spray drying technology centre in the world; we have the expertise and capacity to help you with aspects that are crucial to the success of your product (process development and contract manufacturing under cGMP conditions); working with GEA, spray dried products can be developed without any major capital investment before the product is ready to be brought to market.
China

Working closely with GEA companies, ECUST (East China University of Science and Technology School of Pharmacy) offers direct compression, dry powder inhalation, effervescent tablet pelletization, pellet coating and pellet compression facilities. The laboratory works with pharmaceutical companies to develop new products by offering formulation screening and pilot production with easy scale-up to full production levels. Techniques include taste masking, improving dissolution and bioavailability, developing controlled release and biochemical production. Since GEA entered the Chinese market 30 years ago, it has used its experience to help hundreds of customers to improve products and processes and bring new products to market. The ECUST laboratory provides the necessary equipment and experienced operators to help you do the same.

South Korea

A pharmaceutical process research centre (PPRC) has been established at South Korea’s Sungkyunkwan University (SKKU) using solid dose processing technology provided by GEA. Underlining GEA’s long-term commitment to the region, the centre, known as the GEA-SKKU, will provide academic and commercial research facilities for students and the wider pharmaceutical industry in South Korea. The PPRC will focus on product research and development, process support, trials and training. Research conducted at the centre will include tablet formulation, particle coating and sustained release delivery products.

USA

The GEA Pharmaceutical Test Center (Columbia, Maryland) assists bio/pharmaceutical customers with feasibility tests and partners with them during process development as they move forward from R&D to clinical production, and eventually into full-scale manufacturing. By offering the latest advances in solid dosage processing, our imaginative engineering approach and never-ending stream of innovation has made it possible for us to offer you a facility like no other. The building itself represents the latest developments in pharmaceutical plant design, utilising the through-the-wall concept. This design minimises the clean processing area and allows for technical servicing of the equipment to be done outside the clean area.

Singapore

The GEA-NUS PPRL (Department of Pharmacy Research, National University of Singapore) facility is equipped with a wide range of analytical and pilot-scale equipment. We provide analytical services, scale-up and various aspects of particle/product development and microbiological testing. Collaborative efforts with pharmaceutical, herbal and related industries are strongly welcomed to innovate formulation design and process technology.
GEA has many years of experience in adapting a wide range of technologies and processes into viable solutions for customers who are looking to maximise potential opportunities. Our ongoing development programme constantly examines emerging technologies and their development within the global environment. The test centre staff work closely with our sales divisions, providing an in-depth understanding of current market demands across the entire process equipment portfolio.

A global leader in supplying pharmaceutical equipment, GEA offers manufacturers all over the world the opportunity to enter into a profitable partnership to development both products and processes. The company combines advanced in-house technology with a thorough understanding of the pharmaceutical industry to help customers maximise their development results. Your needs are critical and individual; our worldwide pharmaceutical test centres have been designed to meet those needs.

To improve production quality in the pharmaceutical industry, the US FDA issued the Process Analytical Technology (PAT) document in 2004, stating that the desired goal of the initiative is to design and develop processes that can consistently ensure a predefined quality at the end of the manufacturing process. One of the stated goals is to facilitate continuous processing to improve efficiency and manage variability. PAT is a system for designing, analysing and controlling manufacturing using timely measurements (during processing) of critical quality and performance attributes of raw and in-process materials and processes with the goal of ensuring final product quality. GEA subscribes to the school of thought that states: quality cannot be tested into products; it should be built-in or designed in.

Project management: We’ll find the optimum solution for your individual processing needs. We can assist with single phases of a project or take full responsibility for the design and installation of a complete turnkey plant.

After sales: Regular maintenance is essential to ensure that your equipment operates at maximum efficiency. Fully trained engineers can do on-site servicing and equipment calibration, either as part of a planned maintenance programme or in response to an emergency. Replacement parts can be supplied from stock or manufactured to order. And, we can upgrade existing systems and plant to meet different operational parameters, to comply with changing regulations or for technology transfer.

Training: Equipment operators can undergo training to help them maximise their efficiency, either at the time of installation or periodically as required.

Based on years of experience, equipment qualification is done according to an agreed plan based on documents prepared by us. Our engineers will work closely with your validation staff to successfully qualify your equipment. From plan to complete plant, we’re with you every step of the way.
Granulation remains one of the most important unit operations in the production of pharmaceutical oral dosage forms. And, 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. GEA has long been a pioneer in the development and optimisation of extant and innovative granulation process options.

Single pot technology offers various advantages depending on the product mix; the machine can be cleaned in less than 2 hours; it’s an extremely productive tool for short campaigns or those that require a large number of product changeovers; and, as a single pot operation, it is perfectly suited for the PPE-free processing of potent substances. The advantages of tangential spray systems were recognised by GEA and incorporated into the FlexStream™ multipurpose processor. FlexStream™ eliminates the problem of scale-up and enables completely closed material handling by linking with upstream and downstream equipment. And with the pharmaceutical industry looking at continuous processing to improve production quality in an efficient and cost-effective way — and comply with increasingly stringent regulations — the ConsiGma™ continuous high shear granulation and drying system has been designed to transfer powder into coated tablets in development, pilot, clinical and production volumes in a single compact unit. Continuously producing granules, there is limited waste during start-up and shutdown and the batch size is determined simply by how long you run the machine. Quality is measured throughout the process and, as such, drastically reduces the cost per tablet.

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, such as GEA high shear mixer granulators and fluid bed dryers, we supply plants for cGMP production that are configured to meet the customer’s specific requirements.

For full compliance with national, local and in-house regulations, GEA offers a range of emission control options including solvent recovery systems, outlet filters and full containment plants. Equipment can be supplied to meet explosion-proof and pressure shock standards as required. Our granulation and drying process expertise is based on many years of experience, expertise and know-how. With plants installed around the world and literally thousands of tests performed, we have established a solid base of expertise related to the needs of the pharmaceutical manufacturing industry.

Significant technical advances have been achieved in recent years, enhancing the performance of granulation technology and allowing optimal solutions to be identified for every product mix and production combination. GEA has been a constant leader in the field, driving these developments and endeavouring to provide the right solution for your granulation application.
We live our values.
Excellence • Passion • Integrity • Responsibility • GEA-versity

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.