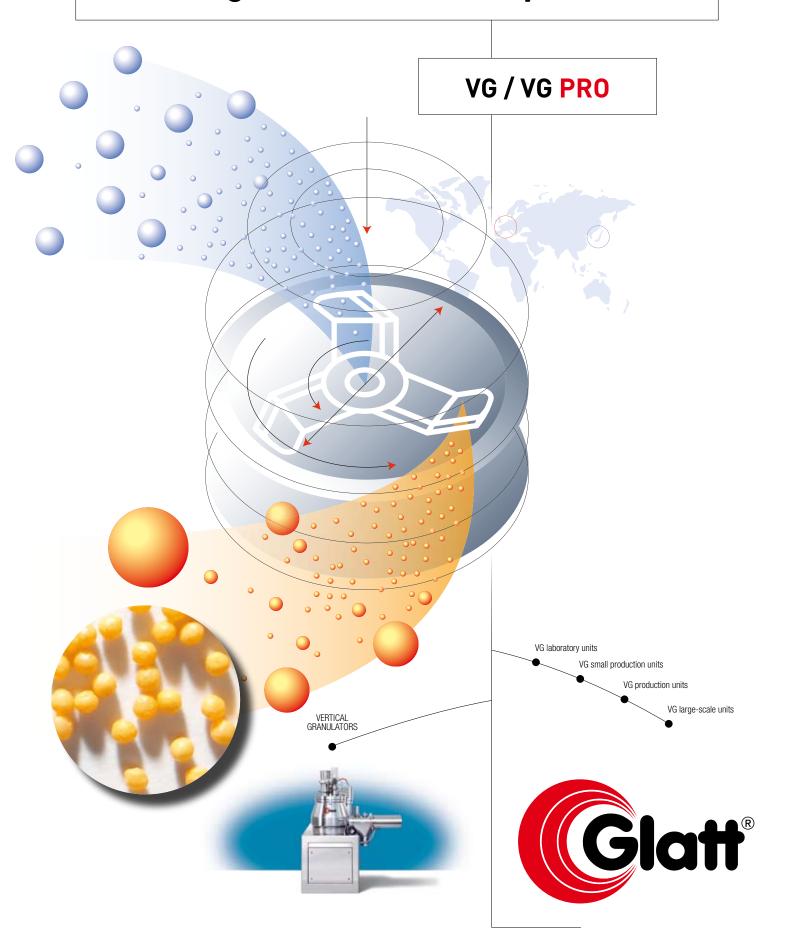
Wet granulation systems



The spectrum of wet granulation

Vertical Granulators from Glatt. State-of-the-art technology.

High shear mixers for wet granulation from Glatt have a history stretching back over decades in the pharmaceutical industry. Today, robust and reliable Glatt vertical granulators are setting a new standard in the pharmaceutical industry. Above all, they are the first choice when the process needs high granulate density and rapid granulation. In addition, they have relatively low space requirements, are simple to operate and – now more important than ever – they are easy to clean. This means innovative Glatt VG technology is best prepared for the future.

Glatt and Powrex. Ensuring progress. Using synergies.



For years now, Glatt has been continuously striving to develop vertical granulators in close cooperation with the Japanese specialist, Powrex. This combined commitment is delivering successes: e.g. the Powrex development of the patented Z-Rotor and SC SuperClean® technology developed and globally patented by Glatt. Equipment has been optimised, allowing differentiated design of the working vessels and the integrated choppers with various tools.

The Glatt Company. Committed to worldwide success.

The Glatt group of companies employs more than 1500 staff in more than 20 companies all over the world. Irrespective of whether the job involves granulating, drying, coating or pelletising, whether you want to produce 100 grams at laboratory scale or several tonnes a day – Glatt machines offer you individual solutions that are tailored to your requirements. Our global service is the cornerstone of Glatt's outstanding brand image.



(2)



VG / VG PRO series

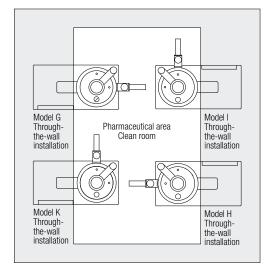
Glatt provides the optimum solution for every requirement.

The extensive Glatt VG range includes a wide variety of standard designs - and therefore the ideal solution is available for every challenge:

- VG laboratory units 1-50 dm³.
- VG small production units 110-345 dm³.
- VG production units 400-1300 dm³.
- $\bullet\quad VG\ large\text{-scale units }1600\text{--}3210\ dm^3.$

In order to meet quite specific requirements as well, Glatt uses existing components to produce tailor-made solutions that are completely focused on the particular task in hand. We do not see spatial requirements as an obstacle, but as a new challenge! In addition, there are various VG wall installation variants for clean room applications.

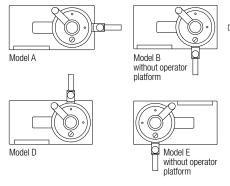
VG / VG PRO. Through-the-wall installation variants.

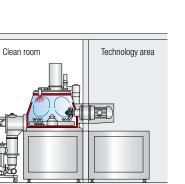


Flexible solutions at no extra cost.

Glatt is more flexible than other suppliers who only have a small product range. Spatial constraints are no problem for Glatt vertical granulators, therefore you will find the exact design to match any requirement. And the best thing is: individual design variants generally do not cost any more than the standard format. An extremely wide range of working vessels for different applications further increases the versatility of the VG range. This means the greatest possible flexibility is boosted by maximum efficiency.

VG / VG PRO. Basic variants.



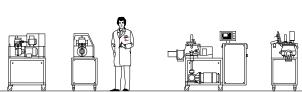


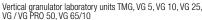
VG clean room through-the-wall installation variant

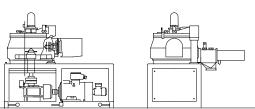




Vertical granulator VG 800 with cylindrical working vessel







Vertical granulator small production units VG / VG PRO 100, VG / VG PRO 150, VG / VG PRO 200

VG / VG PRO designs

VG design.

The classic from Glatt and Powrex.

The VG design is the proven standard machine for efficient granulate and pellet production. It permits wet granulation with a pressure shock resistance up to 2 bar without pressure relief. A particularly efficient production line can be formed by combining this with a Glatt WST Plus fluid bed dryer, sieves, pneumatic conveying systems, etc. The unit is supplemented by a wet sieve on the discharge port for sizing the granules. The proven design of the Glatt VG and its straightforward handling permit perfect integration into existing buildings and systems.

- Efficient basic variant with 2 bar pressure shock resistance.
- Simple handling.
- Perfect integration.



Vertical granulator VG 100

VG PRO design.

The highest dimension of safety.

The PRO design offers all the benefits of the classic VG design. The all-important plus point is the unique pressure shock resistance up to 12 bar without pressure relief. This means there is no need for peripheral safety precautions against explosive overpressure. VG PRO is optimally configured for trouble-free integration in completely closed PRO lines (vertical granulator + wet sieve + fluid bed dryer + pneumatic conveying system).

- All the benefits of the VG design.
- Plus the increased safety of 12 bar pressure shock resistance.



Vertical granulator VG PRO 1200 with opened swinging lid

Options for both designs:

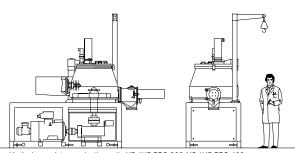
The following special equipment is available optionally for Glatt VG and VG PRO:

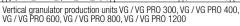
- Vacuum system with solvent recovery / separation.
- Single pot version with heated, jacketed wall surfaces as well as patented gas stripping system through the agitator blades. This means VG and VG PRO are suitable for use in batch operation to manufacture and dry granulates.

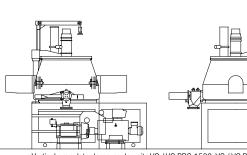


Vertical granulator VG 100, moveable









Vertical granulator large-scale units VG / VG PRO 1500, VG / VG PRO 2000, VG / VG PRO 3000

Technology of wet granulation

Production of solid particles from powder.

In wet granulation, powder is charged into a VG working vessel and the product is vigorously mixed by an agitator and a chopper. Mixing continues while it is then wetted or sprayed with a melt. This process produces denser granulates than in the fluid bed agglomeration process. In many cases, these granules are discharged via a wet sieve to homogenize oversized particles.

Quick and efficient drying.

By nature of the system used, granulates from a VG have to be dried. The combination of a vertical granulator and a fluid bed dryer is unbeatable for high throughput rates. This combination permits maximum efficiency thanks to rapid granulation and effective drying.

VG single pot version for individual batches.

If only single batches or a small number of batches, e.g. high-activity substances, have to be granulated, then the drying process can also take place in a vertical granulator specially equipped for the purpose: using the Glatt VG single pot (see page 6). In this operation, the drying is assisted by suitable measures according to the product and process, e.g. heated wall surfaces, gas stripping and vacuum. The single pot variant is always the first choice, especially for frequently changing products in small and medium batches.

properties of wet granulate:

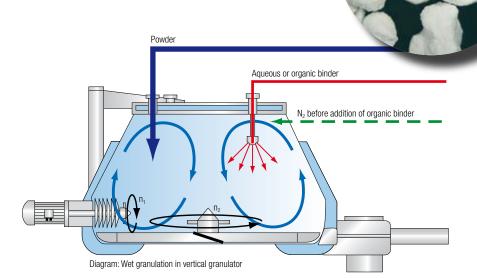
· Dust-free granules.

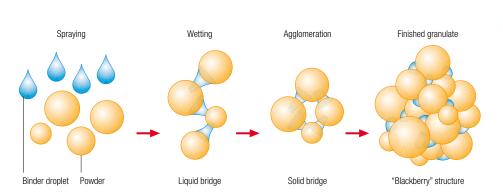
Exemplary product

- · Free flowing properties.
- · Easy dosing properties.
- · Good dispersibility.
- · Perfect solubility.
- Excellent tabletting properties.
- · Compact structure.
- Low hygroscopicity.

Variable application areas for wet granulate:

- Pharmaceuticals.
- Health care.
- · Fine-chemical industries.
- Biotechnology.









VG / VG PRO single pot equipment

VG single pot units. **Product-specific processes** for consistent quality and high-speed drying.

Increasingly expensive ingredients and additives are being used in pharmaceutical research and development. Therefore, the significance and the range of uses for high containment and single pot processes are constantly increasing. Granulation in VG single pot units is appropriate when the following criteria apply:

- · Manufacturing small quantities of wet granulate.
- Frequent product changes with subsequent cleaning cycle (WIP/CIP).
- A completely contained system is required for manufacturing granulates under aseptic conditions with additional sterilisation.

VG PRO single pot units with 12 bar pressure shock resistance.

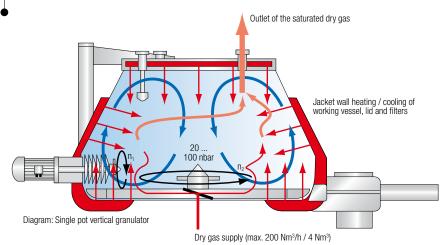
As standard, all Glatt VG single pot units can operate at up to 2 bar over pressure without pressure relief. All VG single pot units are also available in a PRO design with a unique pressure shock resistance up to 12 bar without pressure relief. There is no need for peripheral safety precautions against explosive overpressure.

The VG single pot principle.

Apart from the heat supply through the jacketed wall of the working vessel and lid, the drying phase is additionally accelerated by introducing dry hot air by nozzles which are located on the lee side of the agitator blades. A vacuum is also generated in the working vessel in order to reduce the evaporation temperature further. The process parameters are selected by the control software so that drying is always fast and gentle to the product.

Single pot machines are always the first choice, for example for the following processes:

- · Granulation using wax as the binder solution.
- · Pellet granulation.
- Granulation using organic binder solutions with solvent separation.



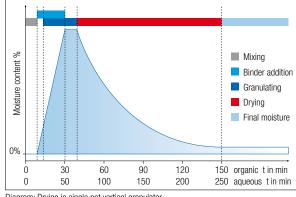


Diagram: Drying in single pot vertical granulator



Working vessel with patented Z-rotor



VG / VG PRO for research and development

Product development and scale up.

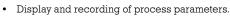
More and more frequently, small and micro batches are being produced from expensive raw materials in the research and development area. Glatt offers VG laboratory units, which can granulate minimum quantities from less than 1 dm3 to 50 dm3 due to working vessels that can be interchanged without using tools.

Universal tabletop mixer granulator TMG.

- Interchangeable cylindrical or conical working vessels with sizes of 1, 2, 4 and 6 dm^3 .
- A cGMP compliant design.
- Space-saving.
- Suitable for integration in isolators.
- Product can be heated / cooled thanks to the jacketed wall.
- Simple charging and discharging.
- · Easy and efficient cleaning.
- Easy-to-operate control system. Display of all critical process
- parameters.

VG 65/10 with interchangeable working vessels.

- Interchangeable working vessels with nominal volumes between 10 dm³ and 65 dm³.
- Working vessels in single-walled or jacketed design.
- Automatic identification of the working vessel size by the control system and adjustment of all parameters.
- Portable with relatively space-saving design.
- Quick and simple start-up.
- Optional use even in potentially ex areas.
- Equipped with industrial PC.
- Proven and simple operation via touchscreen panel.
- Quick and efficient WIP cleaning.









Material flow and handling

Horizontal or vertical – the ideal system for every requirement.

The level of equipment required for a granulation line is generally determined by the product flow. The material flow concept depends on facility conditions such as the existing room space and room height. Product characteristics such as flow properties and the particle size distribution also play an important role. The toxicological data also has to be taken into consideration. Glatt has many different alternatives in its range of products that cover every application.

- Vertical product flow with automatic charging and discharging by means of gravity.
- Horizontal product flow with manual or automatic charging by means of lifting device or pneumatic conveying systems.
- Combination of both material flow concepts.

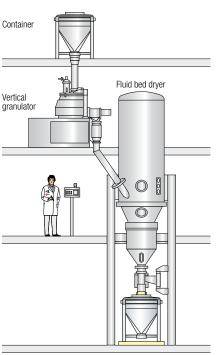
Product discharge with docked bypass tube as an alternative to the wet sieve

Easy charging.

In standard systems, the product charge is fed through a charging port via the vessel lid. The lid of production machines can be opened either by swivelling horizontally or vertically by a drive. In laboratory units, the lid of the working vessel is opened vertically.



Charging via lifting device L 1500 and container, vertical granulator VG 400 $\,$



Vertical product flow in a complete granulation suite for large product throughputs

Addition of the granulation liquid.

Granulation liquid (binder solution) is usually added through nozzle systems fed by means of dosing systems (pressure / eccentric / diaphragm pumps, etc.).



Nozzle for 60° full cone jet



Nozzle for fan jet



Nozzle for 60° / 45° hollow cone jet



Swivelling inline sieve GSF 180 for vertical granulators

Safety and the environment

Consistent reduction in safety risks.

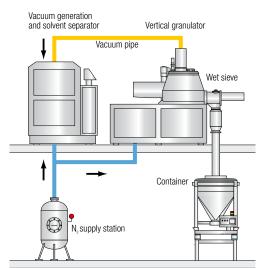
Dust and sometimes organic solvent mixtures represent a major potential risk and are therefore a danger for operators and the machine.

All conventional Glatt vertical granulators are designed to resist pressure shocks of up to 2 bar without pressure relief. With vertical granulators, the explosion risk during production is relatively low due to their design and the nature of the process involved. Product charging and discharging are often more critical with regard to the risk of explosion.

Depending on the particular risk potential, the machine can be fitted with an N_2 inerting system if required. The safety design of all Glatt vertical granulators satisfies the demands of the ATEX-100a Directive and has been certified appropriately.



Vertical granulator VG 100 single pot with solvent recovery / separation



Granulating and drying with solvent recovery / separation

The VG PRO concept. A new global standard for safety.

The VG PRO series sets a new standard with 12 bar pressure shock resistance. This eliminates the known limitations of conventional machines. Explosion pressure relief, all related construction requirements and possible environmental pollution in the case of an accident are topics from the past. Now even critical products can be safely processed in a PRO unit without any additional precautions for pressure relief. With a PRO series closed system, it is possible to produce all the usual pharmaceutical, food, feed and life science products without any difficulties.

VG PRO 12 bar pressure shock resistant.



Vertical granulator VG PRO 1500 through-the-wall installation with working platform

All Glatt vertical granulators satisfy the requirements of the ATEX 100a Directive.

All machines satisfy the relevant regulations such as VDI 2263 and 3673.





TMG laboratory granulator built in an isolator



Control systems / validation

Customised control systems for all production processes.

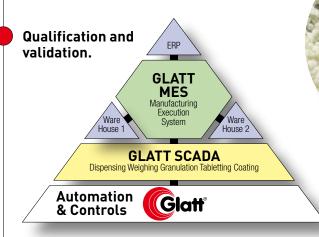
Control systems nowadays often have to fulfil much more complex tasks than monitoring a series of machine functions. Process steps have to be individually configured, critical parameters automatically monitored and the process being performed has to be documented. The process steps can take place with continuation conditions being interrogated and confirmed automatically, or can be performed manually if required.

Predefined, clearly arranged function keys permit easy operation. All messages from the laboratory units are displayed in plain text on a TFT display. All production units are equipped as standard with a large LCD monitor, giving graphical visualisation of all relevant process parameters, including recipe management.

Would you like to visualise and document the entire process sequence, as well as integrating the machine into an overall system? This can be done without problems using the PC based Glatt MegaView controller. We can integrate non-Glatt machines into a shared control concept.

Hardware and software for process controllers of all kinds.

Glatt develops, plans and produces the complete hardware and software for the control systems in-house. This results in a high degree of flexibility with regard to individual customers' requirements. We work with Siemens as the standard PLC, with PC controlled at the next equipment level, if required. For process visualisation, we use well known products such as Intellution, Citect and Wonderware. Explosion-proof control systems are also available for equipment where there is a potential risk of explosion.



The validation procedure begins, according to the existing GAMP guidelines, right from the order placement with the design qualification (DQ), by defining the specifications and test plans according to the customer's requirements. This is followed by the first stages of the installation qualification (IQ), checking that the equipment is complete. After successful installation, our staff perform further validation of the entire equipment and associated software package. The following stages of qualification are performed at the installation location:

- Continuation of the installation qualification (IQ):
 - Correct installation.
- Operation qualification (OQ):
 - Correct function of the equipment.
 - Function of the system in defined working areas.
- Performance qualification (PQ):
 - Reliability of the equipment.
 - Reproducible product manufacturing.

If requested, we can of course also supply extensive documentation for validation, qualification and calibration.



EcoView control panel for stand-alone units



MegaView control panel for integrated units



WIP / CIP / SC SuperClean®

Clean solutions for automatic cleaning processes.

CIP (Cleaning In Place) has become a key topic in the pharmaceutical industry in recent years. Glatt defines a CIP process as a fully automatic, reproducible cleaning process with a defined cleaning result.

WIP (Washing In Place) involves thorough preliminary cleaning and subsequent manual cleaning. It goes without saying that both processes can be validated.

Glatt vertical granulators can be delivered in both CIP and WIP versions. Our range also includes the corresponding CIP / WIP supply racks.



Metal cartridge filter SC SuperClean®



CIP sealing system 0-Plus



Perfect cleaning for all VG PRO. SC SuperClean® technology.

The SC SuperClean® design is Glatt's convincing answer to all questions about CIP in wet granulation. How should problem zones such as the sealing joint, base of the working vessel, underside of the agitator blade or sight glasses be cleaned? What happens in the discharge unit including the docked sieve during cleaning? How can optimum personnel protection be achieved? And above all: how are filters cleaned to a defined standard?

Glatt has developed a perfect solution for each specific problem and has brought them together in the SC Super-Clean® series. For example, the filter cartridges are cleaned by cyclic pressure shocks during the ongoing process. The integrated wash nozzles can be used for fine cleaning after lengthy operation or after product changes. Optionally, every PRO machine can be equipped with SC SuperClean® technology that leaves the competition standing.





WIP cleaning station for non-reusable cleaning



Extendible washing nozzle

Total containment

Maximum safety for people, products and the environment.

Processing highly effective and critical substances demands extensive protective measures for personnel and the environment. Special requirements are placed on the machine technology to provide your staff with complete protective equipment. This involves complying with the occupational exposure limit (OEL) level as well as closed cleaning of the machine after a process.

The latest technology – units with 12 bar pressure shock resistance.

Closed PRO machines with 12 bar pressure shock resistance are used in total containment systems. All the seals are designed for this purpose. Integrating processing machines on the charging and discharging sides with 100% gas-tight seals demands corresponding expertise. There is no reason why processing machines from well known machine manufacturers cannot be integrated.

Closed product flow. Charging and discharging.

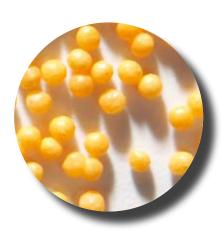
Charging and discharging must take place under totally dust and contamination-free conditions. This represents a challenge, particularly when docking and releasing containers.



Charging with total containment flap system

Contamination-free flap system for perfect total containment.

In order to prevent any cross-contamination, we use a contamination-free valve system especially developed for this task. The patented design prevents substances from being released in an uncontrolled manner and avoids contamination of the processed product.





Accessories / services

Individual, tailor-made service package.

Glatt offers a complete package of machinespecific accessories and services so that your vertical granulator can be used optimally. From handling equipment such as sieves, lifting devices, containers, container mixers, isolation valves, weighing systems included the related training programmes for your workforce. Some examples:



GPCG 60 PRO for drying, fluid bed granulation and coating



CM 400 container mixer with docked rotor sieve GS 180







LD 120 lifting and discharging device

Process and product development.

Clinical samples, scale-up and cGMP, complete product development or optimisation with the latest technologies through to system comparisons, all under GMP conditions of course. The Glatt Technology Centre with its extensive range of systems and machines as well as the modern analytical laboratory offers you a complete range of services for research, development and production. This is backed up with all the expertise gathered during 50 years of experience in process engineering.

Engineering.

We integrate our machines into your building. Glatt is also your expert partner for process lines and overall concepts as well as turn-key planning.

Seminars and training courses.

We train your operation and service personnel under practical conditions - even before your machine is delivered. This saves time and money. A practically oriented range of training courses is on offer for your engineers and operators within the framework of our TTC programme. It is an ideal platform for users to exchange their experiences.

Installation, start-up, service.

We offer you a comprehensive service from installation through to start-up and regular maintenance, so that your machine can start operating quickly and without problems. For example, many spares and parts subject to wear can be delivered at short notice.

As you can see, we do our utmost to make you successful. After all, your success is also our success!



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