

Mixing and Granulation



Aeromatic-Fielder Technologies

GEA Pharma Systems is world leader in providing advanced processing solutions for solid dosage forms to the pharmaceutical industry. Based on a dedication to research and durable quality, GEA Pharma Systems offers a wide range of solutions, from individual pieces of equipment to complete integrated plants, by uniting the state-of-the-art technologies of Aeromatic, Buck, Collette, Courtoy, Fielder, Lyophil, Nica and Niro.

Product Know-How



Process Expertise

For more than forty years, Aeromatic-Fielder has supplied advanced solids processing plants for blending, granulating, drying, pelletizing and coating to the pharmaceutical industry. This includes small capacity systems designed for R & D as well as industrial size plants for batch production of pharmaceutical compounds under cGMP conditions.

Our plant and process expertise is based on experience and R & D. 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.

Delivering the Right Solutions

Every Aeromatic-Fielder plant begins with the customer's desire to create a product that will succeed in the market. In Aeromatic-Fielder, the customer finds a partner who will assist him to meet that goal. Our expertise includes technologies for processing Active Pharmaceutical Ingredients using, Blending, Granulating, Drying, Pelletizing and Coating.

Plants Customised for Success

Every pharmaceutical plant and system from Aeromatic-Fielder is a unique union of proven technology and individual solutions. Based on standard components, we supply plants for cGMP production configured to meet the customer's specific requirements.

A Partnership in Every Perspective

Working with Aeromatic-Fielder means entering a solid partnership every step of the way, from process testing and design to specification of the software controlling your new plant. And our comprehensive after sales program ensures that your return on investment is optimised throughout the lifetime of the plant.

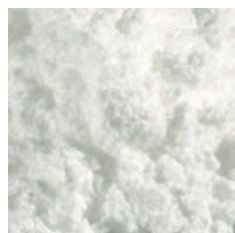
Safety and the environment

For full compliance with national, local and in-house regulations, Aeromatic-Fielder 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.



Process Technologies

The High Shear Mixer/Granulator is a multi-purpose processor equally suitable for high speed dispersion of dry powders, aqueous or solvent granulations, effervescent products and melt pelletization.



Dry Mixing

High Shear mixing consists of a fast homogeneous blending of active powder and the excipients using a high-intensity mixing blade.

Special features

Evaluation of blend homogeneity by NIR-Technology

Wet Granulating

The high shear granulation process combines the active powder and the excipients with a binder solution using a high-speed mixing blade and chopper.

Special features

Control of granulation process via in-line focus beam reflection measurement

Melt Granulating

Melt agglomeration is a process by which agglomeration - or size enlargement by which fine particles are bound together to agglomerates or granulates - is obtained through the addition of either a molten binder liquid or a solid binder which melts during the process. Agglomerates are formed by agitation of the mixture. To obtain a stable, dry granule, a cooling to ambient temperature is necessary to solidify the binder.

Dry Bonding

When low amounts of drugs should be administered via inhalation, the accuracy of current devices is not precise enough. Therefore the small drug particles are bonded to the coarse surface of lactose particles in a dry high shear process. This requires special technology - Aeromatic-Fielder's expertise in this process provides; special impellers giving enhanced shear forces, loading systems allowing a precise layering of drug and excipient and often special containment devices such as Buck® split valves or Hicoflex™.

Effervescent products

One granulate method using water

A very small amount of water is added to start the pre-effervescent reaction by which some of the carbon dioxide is released during granulation, but by which 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 dryer by discharging at the end of the granulation process the material into a pre-heated fluid bed dryer.

Built-in Versatility

Pelletizing

To form granules out of powders a granulation liquid and mechanical energy is needed.

Wet Pelletizing

This process uses a Niro Rotary Atomiser spray to achieve excellent dispersion of binder liquid through the mix, and a special high-speed rotation blade for maximum movement of the product, for more efficient pelletization. A PTFE container-lining minimises the need for 'top and tailing', even with the most cohesive of products. Studies have shown that the PTFE liner - unique to Aeromatic-Fielder - can increase production efficiency by as much as 40%. Alternatively, an extruder may be used, similar to those used for the manufacture of pellets. In a typical set-up all ingredients are pre-blended in a container after dispensing. Depending on the extruder design the liquid can be added in the extruder or mixed separately to the correct consistency.

The material produced by the extruder is now not rounded in a spheronizer (as it would be for pellet manufacture) but transferred directly into a continuous fluid bed where it is dried to the desired moisture level.

Melt pelletization

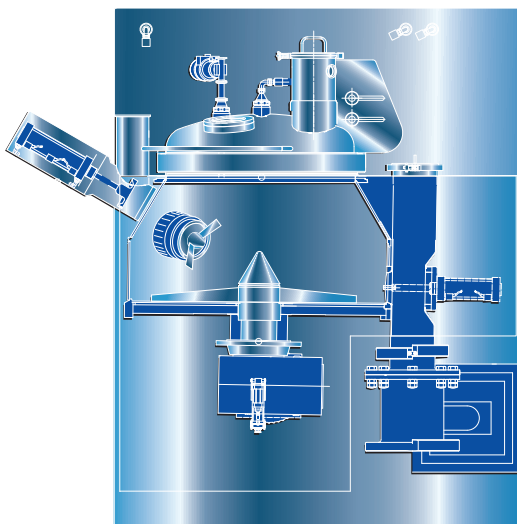
This is an exceptionally fast method of producing pellets in a single step. The active material and binder are mixed in binder form then heated until the binder melts. A single batch is processed typically in just 15-20minutes, and needs no further drying.



PMA-Standard & PMA-Advanced™

High Shear Technology

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



Through-the-wall configuration

Through-the-wall offers the best option in terms of cleanliness, maintenance and ATEX. By keeping the motors out of the process room, you are preventing risk of contamination coming from these difficult to clean items.

Maintenance is carried out from the technical area, minimising the need for the maintenance engineer to work in a GMP area. This makes the job easier and again reduces the risk of contamination. For ATEX, the design allows us to classify the technical area as safe. This avoids the need for costly flameproof motors, making the upgrade for working with solvents much easier.

The frame mounting provides a standard format for the machine, allowing it to be constructed and installed using the same structure. This structure may be raised using standard modules to achieve the customer's desired height. For some installations it is also possible to mount control panels on the structure, allowing qualification of the complete system prior to shipping, significantly reducing the installation time on site.

Impeller & chopper options

Standard PMA impeller:

Standard impeller designed for use with the conical bowl of the PMA high shear granulator.

U-Shaped chopper:

Standard chopper for use with the conical bowl of the PMA high shear granulator.

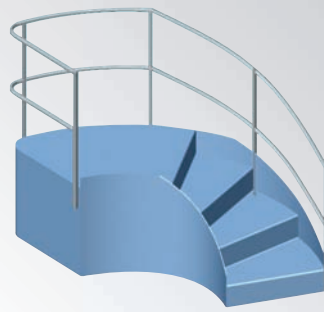
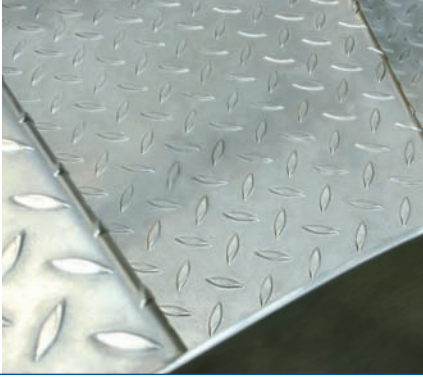
M8 impeller:

Innovative swept-back design; for improved mixing characteristics, faster processing and a more clearly defined end-point.

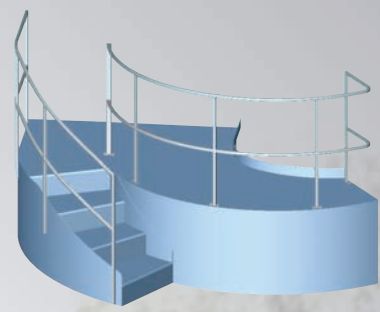
Multi-bladed chopper:

Flush mounted, multi-blade design improves binder solution dispersion and product movement at slow speeds.





“Medium” platform



“XL” platform

Filtration

Material filter & shroud

Production filtration is achieved using an easily removable material filter that can be cleaned and re-used. For vacuum and CIP applications stainless steel may be utilised.

Discharging

Through-the-wall mill

Product can be discharged from the high shear granulator directly into a receiving container, or via a sizing mill. This breaks down the granules to produce more even sizing for subsequent processing.

The PMA-Advanced™ features a through-the-wall hinge-mounted sizing mill, directly connected to the discharge port, using inflatable seals. For maintenance, cleaning and product changeovers, the seals are deflated and the mill hinged away from the port, allowing full access.

The TTW mounting ensures the motor and controls are kept away from the clean process area.

In addition to the standard mill, CIP and Pressure Shock Resistant options are available, matching the containment and safety credentials of the main machine.

Concealed hinge mechanism

The cover is mounted on a concealed hinge mechanism allowing the cover to be lifted with the minimum effort, but keeping the counterweight in the technical area. This leads to a more GMP design, reducing surfaces, making cleaning easier. On equipment supplied with the Pressure Shock Resistant design option the hinge interlocking system is power assisted to provide safe and comfortable opening to the bowl cover.

Loading

Gravity loading

Simple open / close ports may be mounted on the cover and used to dispense product into the mixing bowl. For potent powders, split-valve technology provides full containment during loading. The PMA-Advanced™ can also be delivered with a cone loading port, allowing for

the removal of the powder loading ports from the cover, but giving permanent connection to a Gravity Loading Station, but also continuous access to open the cover.

Vacuum loading

Rapid loading can be achieved using vacuum technology. Aeromatic-Fielder's innovative killed-vacuum technique makes for easy operation and maintenance, and only requires a standard-sized filter.

Binder solution addition

Nozzle

A range of nozzles are available to give the optimum binder liquid droplet size for an even distribution throughout the powder mass.

Pump

The binding solution required for granulation may be pumped into the mixing bowl using a mechanical or peristaltic pump to deliver the binder liquid to the spray nozzle. Special pumps are available for the dosing of high viscosity binders.

Pressure pot

Alternatively a pressure pot offers fast, high-pressure delivery of the binder solution, for excellent dispersion of liquid via the binder nozzle spray system. These systems are chosen typically for small scale, R&D-sized granulators.

Standard Platform Designs (optional)

Two standard platforms are available to integrate with the PMA-Advanced™. The “Medium” platform provides room adjacent to the bowl for the operator to carry out all filling and cleaning operations. The “XL” platform additionally provides space for other items / operators on the platform and also provides sufficient space to allow the operator interface to be mounted at the platform level.

Due to the clean lines of this design the bowl/ cover area can be easily accessed using mobile steps. Additionally we can offer bespoke platform design and construction services to provide the optimum integration within the available plant area.



In process measurement position



Clean and calibrate position

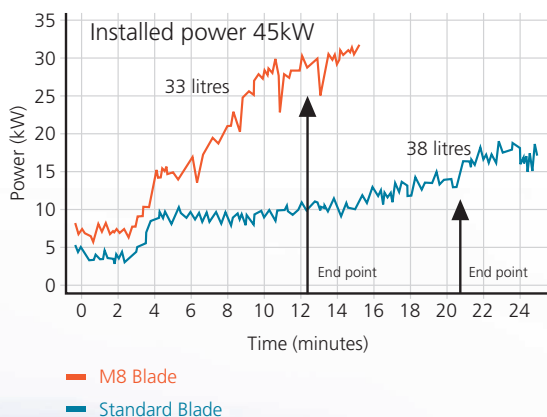


CIP position at end of process

End-point control

A choice of automated end-point control facilities, with trending for process optimization, is offered with all of the system control options - manual as well as PLC-based. Options include fixed process time, automatic end-point control based on power consumption, and a high-accuracy torque-based system. Both the power- and torque-based options can be used to optimize spray rate and wet massing time, for faster, more uniform granule growth.

It is also possible to control in-line the growth of the granules with FBRM.



Granulation comparison

Insoluble active

Granulation graph showing the improvements gained in a straight walled vessel when using the M8 impeller, include reduction in binder solution, reduced granulation time and enhanced end-point definition.

Lighthouse Probe™ Technology

GEA Pharma Systems (GPS) has joined forces with J&M GmbH to create a compact and cleanable in-process optical probe for use in powder processing equipment.

The result is the novel Lighthouse Probe™, which can be used with a range of spectroscopic techniques, including NIR and UV/vis, to overcome the traditional problem of product sticking to observation windows.

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 new GPS & J&M Lighthouse Probe™ has overcome this problem.

Sizes & Capacities

Proven Process

Critically the process geometry of the PMA-Advanced™ is identical to the previous model. Modifications to the design have been made solely to benefit the user and owner in terms of ease-of-use, cleanability, process analysis and installation. By uniting these new benefits with the proven PMA process technology, Aeromatic-Fielder is providing the logical solution for your Granulation Needs.

Standard options configured into tailor-made plants

The philosophy behind the design is that a combination of standardised options are built together in order to meet the requirement for a specific duty. Therefore, granulators of equal capacity may be completely different with respect to design, configuration and physical size.



Production capacities

		PMA150	PMA300	PMA400	PMA600	PMA800	PMA1200	PMA1800
Bowl Volume	Litres	150	300	400	600	800	1200	1800
Typical Weight@ 0.6 g/l	kg	60	120	160	240	320	480	725
Main Impeller	kW	11	22	30	30	36	45	75
Mixing Impeller (variable speed)	rpm	5-260	5-220	5-200	5-170	5-160	5-140	5-120
Granulator Motor	kW	4.0	7.5	7.5	11	11	15	22
Granulator Speed	rpm	1000 - 300	1000 - 300	1000 - 300	1000 - 3000	1000 - 3000	1000 - 3000	1000 - 3000
Weight (approx)	kg	1000	1800	1900	2200	3200	4000	6000



Lab / Pilot capacities

		PMA1	PMA25C	PMA65C
Bowl Volume	Litres	3 / 7.5 / 10	25	65
Typical Weight@ 0.6 g/l	kg	1.2 / 3 / 4	10	26
Main Impeller	kW	3	5.5	7.5
Mixing Impeller	rpm	300-1500	50-500	40-400
Granulator Motor	kW	0.15	1.3/1.8	1.3/1.8
Granulator Speed (50 Hz)	rpm	1000-3000	1500/3000	1500/3000
Granulator Speed (60 Hz)	rpm	1000-3000	1800/3600	1800/3600
Weight (approx)	kg	230	640	665

Integration

Optimum Process Efficiency

Current Good Manufacturing Practices increasingly require that product is fully contained during processing to protect operators and environment. Integrated process systems not only offer containment but improved productivity through automation, increased yield and efficient cleaning procedures.

System integration

GEA Pharma Systems specialises in the design and manufacture of fluid bed and high-shear granulation technology and is uniquely qualified to provide state-of-the-art integrated high shear mixer-granulator and fluid bed drying technology. Drawing on its world-class expertise, GEA Pharma Systems offers fully integrated turnkey installations. The service includes: design, installation assistance, commissioning, process validation, as well as training, and technical support. Installation, operation qualification and documentation are carried out according to FDA/GAMP guidelines.

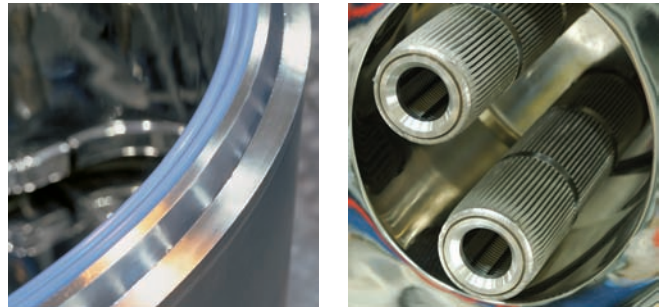
Integration by design

Aeromatic-Fielder's entire range of process equipment is designed with system integration in mind. A modular approach allows customers to select standard process modules to suit project needs. 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, filtration units, all designed for fully integrated systems. Safety, containment, product flow and building requirements are in-built for full integration for optimum process efficiency



Cleanability & 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 Aeromatic-Fielder has developed a unique approach to CIP.



Shaft seals provided in a “cartridge” design for easy removal and replacement.

The shaft seal symbolises, the many developments that the PMA has seen over its existence. The PMA-Advanced™ utilises a cartridge-mounted seal system that exhibits excellent performance for efficacy, clean-down and wear-life, without the need to purge compressed air through the seal and into the process. Maintenance benefits include rapid replacement and condition monitoring.

Clean line discharge valve

The circular discharge chute design is based on “quick exit” and clean drop of granule with minimum “hang up” surfaces. The discharge valve has evolved to ensure the minimum of surfaces are exposed to the product, making it simple to clean, either manually or as part of a CIP recipe.

Concealed Services (optional)

The Filter system can be mounted in the hinge mechanism with exhausted air passing through the centre of the hinge. This creates a less cluttered working space with fewer hoses being run in the process area to the machine. Furthermore pneumatic pipework for actuators and other similar services may also be run through the hinge.

CIP* and WIP

All the high shear granulation systems can be supplied with a wide range of washing-in-place and fully automated cleaning-in-place options. CIP features include a combined vacuum cover seal which prevents product leaks, lifting impeller, automated spray head and filter cleaning, and internal O-ring seals.

*CIP patent



Continuous Improvement

Safety

Improved safety for integrated granulation and drying suites

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

Safety when using organic solvents

The tests were carried out with hybrid mixtures that behave in the same way as pharmaceutical products containing organic solvents and showed that the final explosion pressure in the granulator is dependent on the volumes of the two vessels and that the length and diameter of the interconnecting duct is critical in ensuring that the pressure remains within safe limits.

The tests showed that where the fluid bed is designed in accordance with VDI 2263 part 5 (i.e.: for a 10-bar explosion pressure, which the standard considers to be adequate for all pharmaceutical powders and organic solvent combinations), then the granulator must be able to withstand an over pressure of at least 16 bar to provide a range of transfer duct configurations which are both practical and safe.

Where the fluid bed is required to handle materials with explosion pressures greater than 10 bar (e.g.: metal powders) - and hence is designed outside of the VDI standard - or where the configuration of the interconnecting duct is outside the safe design parameters, then either the granulator must be designed to a higher pressure shock resistance or a

hygienic fast acting valve, or some other form of protection, is essential. The test program showed that the pressure enhancement effects are caused by the difference in the propagation speed between the pressure wave and the flame front. The worst cases are when the pressure in the granulator is able to rise significantly before the flame can reach it and ignite the pre-compressed material. For the range of transfer duct configurations to be used with the 16-bar granulator design, the presence of bends and obstructions such as mills was not seen to affect the increase in pressure.

For plant processing powders, or mixtures that are not flammable at the time of transfer between the granulator and the fluid bed, then the risk of explosion is eliminated and hence a wider range of transfer duct designs can be used safely. This extensive research program has significantly advanced the state of the art in safety technology for pharmaceutical plants and confirms GEA Pharma Systems' commitment to introducing new products which are based on sound research and development using solid process know how and understanding.

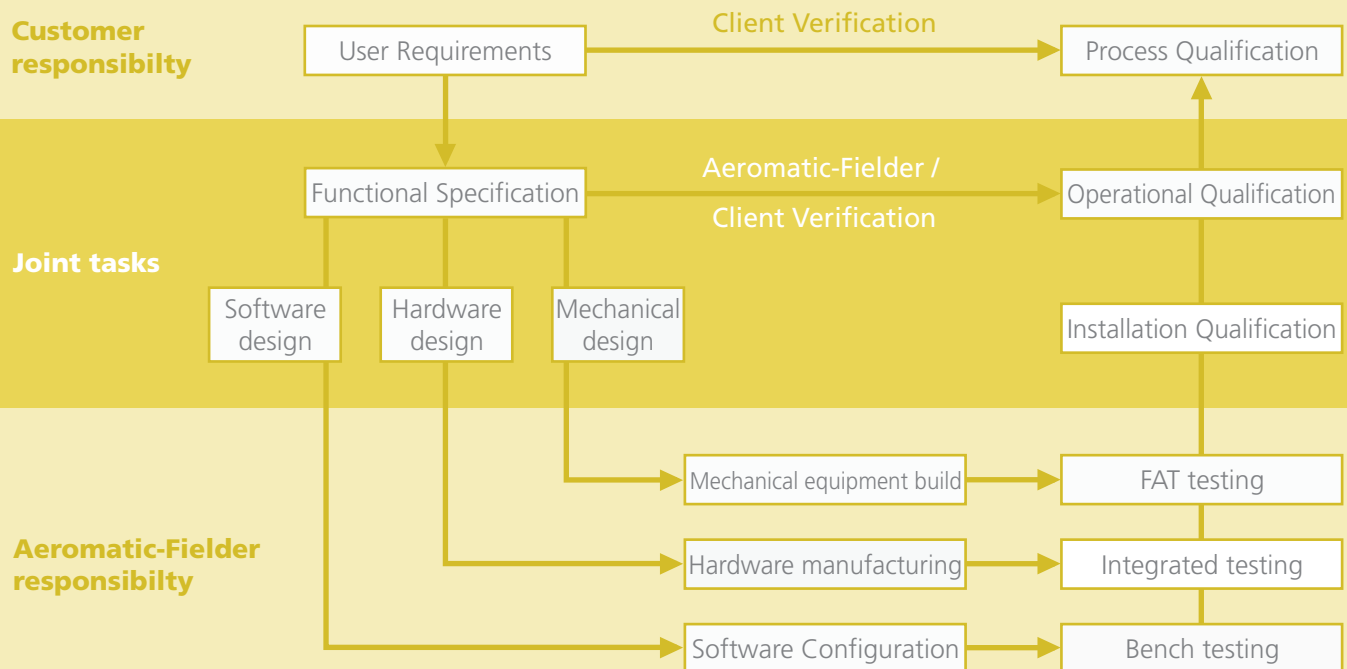




The Complete Partnership

Working with you...

Entering a partnership with Aeromatic-Fielder means entering a partnership that does not end until you are completely satisfied. From the moment you have specified your user requirements and until the plant has been put into service and has been qualified, our trained staff stays with you at every step of the process, working in close co-operation with your own staff creating the components and systems that will result in a finished plant.



...Every Step of the Way

Based on years of experience, equipment qualification will be carried out according to an agreed plan using documents prepared by Aeromatic-Fielder.

Our engineers will contribute to a successful qualification of the equipment in close co-operation with your validation staff.

Service for Life



Project Management

The expertise of the Aeromatic-Fielder engineering team is available to help customers find the optimum solution for their individual processing needs. The company assists with single phases of a project, or takes full responsibility for design and installation of a complete turnkey plant.

Training

Operators of Aeromatic-Fielder equipment can undergo training to help them maximise efficiency, either at the time of installation or periodically as required.



After Sales

Regular maintenance is essential to ensure equipment operates to maximum efficiency. Fully trained engineers can carry out on-site servicing and calibration of equipment, either as part of a planned maintenance programme or in response to customer need. Replacement parts can be supplied from stock or manufactured to order.

To avoid the expense of equipment replacement Aeromatic-Fielder can upgrade existing systems and plant to meet different operational parameters, to comply with changing regulations, or to modify for use at another location.



Central Know-How on a Global Scale

Based on a strong commitment to research and development, pharmaceutical technology centres in Belgium, Denmark, Switzerland, the UK, Singapore, and USA provide global technical support and know-how to the pharmaceutical industry. These centres

of excellence give customers access to a range of test facilities and expert teams with technical and process know-how. Our teams work closely with our customers to optimise processes and evaluate their products, enabling them to achieve their process and production goals.



Contracting Profitable Experience

A world leader in supplying pharmaceutical equipment, GEA Pharma Systems offers manufacturers all over the world the opportunity to enter into a profitable partnership for development and contract. GPS combine advanced in-house technology with a thorough

understanding of the pharmaceutical industry to help customers maximize their development results.



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