



GEA Niro Pharmaceutical Spray Drying

Improve drug properties and
production with spray drying

Industry-leading technology

Spray drying is a technique preferred by a growing number of pharmaceutical companies to produce better drugs. This ultra-fast and gentle drying technology offers unique possibilities for designing particle characteristics. You can see examples on the following pages.

For eight decades, GEA Process Engineering, through its GEA Niro brand, has been a pioneer in all aspects of spray drying and has contracted and installed more than 10,000 plants worldwide. The GEA Niro Test Centre is the world's largest and most advanced spray drying technology centre with a GMP* Pharmaceutical Spray Drying facility approved according to European Medicines Agency (EMA) regulations since 2004.

Traditionally, the pharmaceutical industry has relied on batch production processes. Only recently has continuous processing come into focus as a means of extending production time and ensuring consistent quality. By nature, spray drying is a continuous process and is designed to not only offer high productivity, but also uniform product quality over sustained periods.

**GMP: Good Manufacturing Practice. Guidelines and regulations given by US Food and Drug Administration (FDA), EUDRALEX (EU) or International Conference on Harmonization (ICH).*



GEA Niro SDMicro™ R&D and laboratory spray dryer. Nominal drying gas rate: 30 kg/h.



Standard GEA Niro PHARMASD™ type PSD-1 spray dryer for closed-cycle operation with solvent-based feeds. Nominal gas drying rate: 80 kg/h.

Powder collection in clean room, custom-designed PHARMASD™ type PSD-4.



World-leading expertise

Regardless of the size of your organisation, GEA Process Engineering experts are well prepared to match the services you require. From feasibility testing during initial R&D, to the production of your Investigational Medicinal Product (IMP) for clinical trials, GEA Process Engineering is your partner. When you are ready to purchase your own spray dryer, GEA Niro spray dryers are offered with instrumentation and designs that can document reproducible results for later approval procedures. GEA Process Engineering can fulfil your need for a production spray dryer for excipients, Active Pharmaceutical Ingredients (API) or finished drug products with our standard or custom-designed plants.

GEA Process Engineering delivers far more than the stainless steel components that our plants consist of. We help optimise the composition of the liquid feed and the complete spray drying process. During design and project execution, we follow up-to-date quality procedures (ISO 9001:2008 certified) and the GMP spray dryers are delivered with full Factory Acceptance Test (FAT) documentation. Depending on your preferences, we can recommend one of our standard plants, or design a custom plant based on User Requirement Specifications (URS). Customers may choose to manage plant erection and commissioning alone, or with any combination of assistance from GEA Process Engineering. Recognising GEA Process Engineering as the experts in spray drying, many of our customers ask us to prepare the qualification protocols to follow when validating the installed plant. For a Site Acceptance Test (SAT), Installation Qualification (IQ) and Operation Qualification (OQ), GEA Process Engineering project engineers are ready to assist you.

Customers are serviced round the globe by local GEA companies, several of which have their own spray drying group.



GEA Niro PHARMA SD™ type PSD-4 chamber and HVAC ducts.

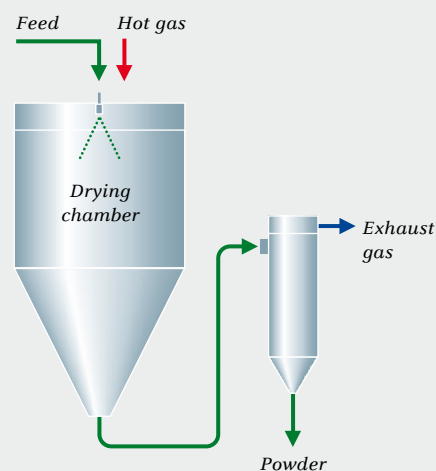


Since 1997 GEA Niro pharma has been certified to conform with ISO9001 standards.

The spray drying process

As a technique, spray drying consists of three basic stages:

- A. **Atomization:** A liquid feed stock is “atomized” into droplets by means of a nozzle or rotary atomizer. Nozzles use pressure or compressed gas to atomize the feed while rotary atomizers employ an atomizer wheel rotating at high speed.
- B. **Drying and particle formation:** Guided by a gas disperser, hot process gas (air or nitrogen) is brought into contact with the atomized feed, initiating evaporation. As the liquid rapidly evaporates from the droplet surface, a solid particle forms and falls to the bottom of the drying chamber. The balance between temperature, flow rate and droplet size controls the drying process.
- C. **Recovery:** The powder is recovered from the exhaust gas using a cyclone or a bag filter. The whole process typically takes no more than a few seconds.



Five ways spray drying can help you commercialise discoveries

1. Increased bioavailability

Many modern therapeutic compounds are stable in a crystalline form but often display poor aqueous solubility, and with this, low dissolution rates. This reduces the bioavailability of the API, sometimes to the point of nullifying the therapeutic effect.

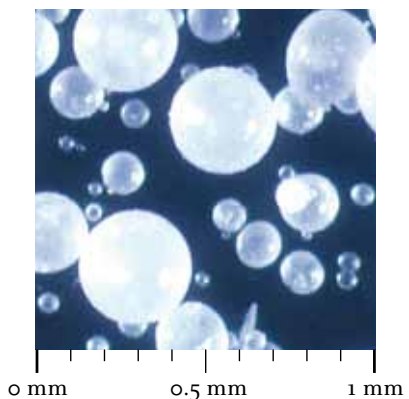
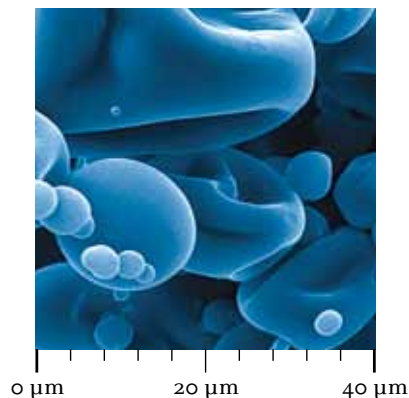
With spray drying, it is possible to co-precipitate an API with a polymer into a stable amorphous solid dispersion, thereby greatly improving the dissolution rate. Specifically, it is the unparalleled drying rate that enables the API to be captured in amorphous form.

An interesting technique for improving the dissolution rate is to create nanoparticles that are isolated and then recovered by the spray drying process. By enhancing the dissolution rate in this way, spray drying has the potential to make treatments possible that are currently unfeasible due to low bioavailability.

2. Modified release and taste masking

Encapsulation offers a number of commercial and medical advantages. It allows the sustained release of, e.g., antibiotics, reducing dosage requirements. By preventing drug concentration peaks, encapsulation is also an effective way to treat chronic illnesses with reduced side effects. Taste masking and the physical protection of the API are other common applications.

Spray drying makes it possible to engineer particles to create specific release patterns and other desired properties. For encapsulation, the API and biodegradable excipients are dissolved and/or suspended. Subsequently, the feed is atomized and dried into a powder.



An interesting alternative approach is spray congealing. Here, the API is melted or mixed with molten excipient and the powder particles produced by atomization and cooling.

3. Aseptic production

Aseptic spray drying offers a number of advantages over traditional methods of aseptic drying like lyophilisation. Spray drying provides more control over the drying process and, as a result, over the shape, density and morphology of the final product. Lower running and capital costs also mean reduced overheads.

Production of dry sterile dosage forms often involves mixing the API with one or more excipients. To achieve a homogeneous mixture, the particle size distribution of the excipient(s) must match that of the API. In a one-step operation, spray drying can turn a sterile solution into sterile particles of the required size without any risk of introducing impurities - a well-known problem with milling.

4. Products for inhalation

Inhalation is a pain-free and self-administrable delivery method and for these reasons is often preferred by patients and medical professionals. However, remarkably few inhaled powder treatments exist. The main reason for this is that although producing powders for inhalation is relatively easy on a small scale, it has been hard to replicate at a commercial level - until now.

Using our knowledge of drying and formulation, GEA Process Engineering has developed highly specialised GEA Niro spray drying nozzles that give you far greater particle engineering capabilities, even on a large scale, making it possible to accurately manipulate aerodynamic particle size and flow properties.

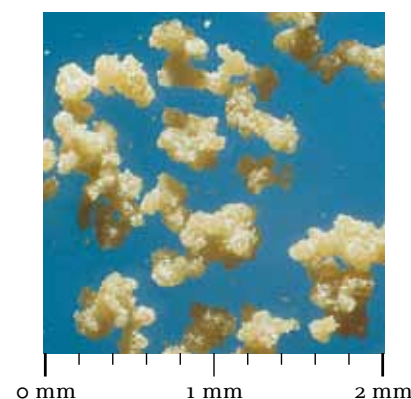
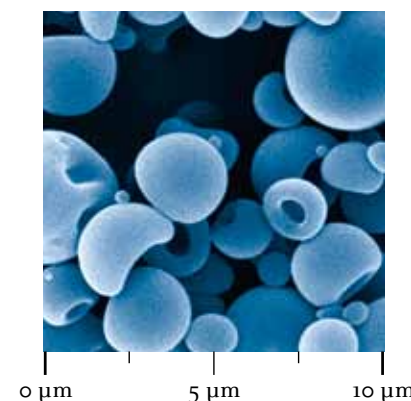
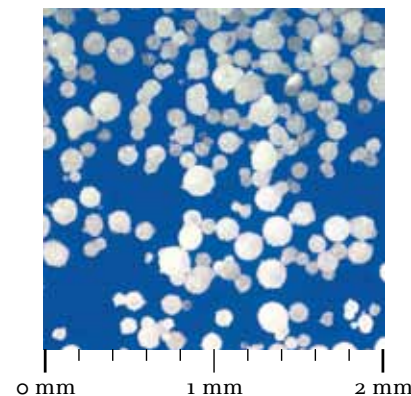
Consequently, our technology makes it easier than ever before to efficiently produce therapies in the form of free-flowing particles of a small aerodynamic size, suitable for inhalation.

As a delivery method, inhalation is particularly relevant for commercialising biological compounds such as hormones, peptides and proteins that risk degradation if ingested.

5. Direct compressibility

Solid dosage pharmaceuticals often require a separate granulation step in the production cycle to avoid segregation and to produce a powder with flow properties that can accommodate a high-speed tablet press.

With the GEA Niro Fluidized Spray Dryer – FSD™ concept, the granulation step can be made an integral part of the continuous drying process - a technique pioneered by GEA Process Engineering. The FSD™ technology can also achieve low residual volatiles content in the final spray-dried powder. The result is a more streamlined, efficient production process and reduced costs.



Five things you might not know about spray drying

1. Spray drying is suitable for heat-sensitive materials

Spray drying is used for processing heat-sensitive materials on an industrial scale. The thermal energy in the hot process gas is immediately consumed by evaporation, keeping droplet temperatures at a level where no harm is caused to the product.

2. Spray drying turns liquid into particles within seconds

The large surface area of the droplets provides near instantaneous evaporation, making it possible to produce particles with amorphous structure.

3. Spray drying is relatively easy to replicate on a commercial scale

With well over half a century's experience, our process know-how, products and exceptional test facilities put GEA Process Engineering in a unique position to manage the scale-up process.

4. Spray drying is a robust process

Spray drying is a continuous process. Once the set points are established, all critical process parameters are kept constant throughout production and all information is fully traceable.

5. Spray drying can be effectively validated

Quality-by-Design is an integrated way of working for GEA Process Engineering specialists. GEA Process Engineering has extensive experience of supplying GEA Niro spray dryers and processes that have been validated and approved by regulators. The precise control of all critical process parameters in spray drying provides a high degree of assurance that the process consistently produces a product that meets set specifications.



The controlled atomization used in spray drying technology offers unique alternatives for drug formulation and particle design.



Two-fluid nozzle dedicated for large scale GMP production of very fine particles. (Patented)



Rotary atomizer F1.5 X designed to meet cGMP requirements. (Patented)

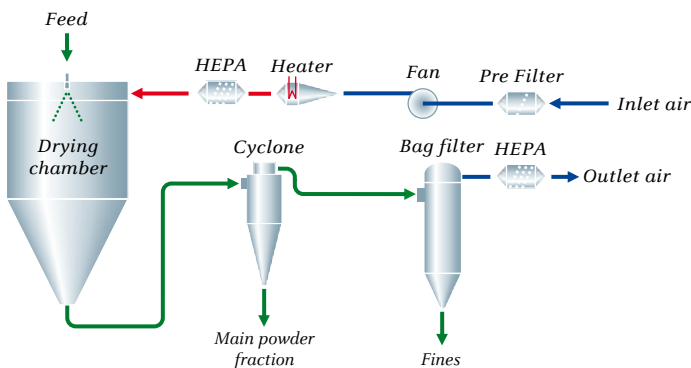
We care about your well-being

The patient is the ultimate focus of any pharmaceutical company, but safety in medicine manufacturing is of great importance too. That's why every GEA Niro spray drying project begins with a risk assessment, incorporating preventative measures at every step of the process.

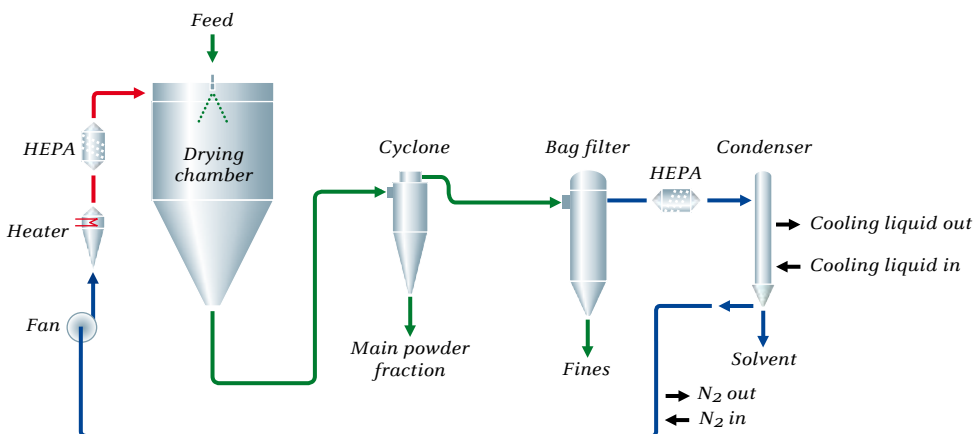
We eliminate the obvious risk of explosion posed by organic solvent(s) by using nitrogen as a process gas and, in large plants, recycling the gas through a closed-cycle system. Less obvious is the risk posed by organic powders suspended in atmospheric air and again we may address this risk by using nitrogen. However, depending on the characteristics of the powder, other solutions are available, such as venting panels or automatic explosion suppression systems.

Nitrogen also provides the answer to a third issue: the sensitivity of certain drugs to oxidation, no matter whether the feed stock is solvent or water-based. Although spray drying is a fast, gentle process, some powders require immediate cooling to room temperature. GEA Process Engineering offers different designs for cooling the continuous powder stream.

Once-through configuration



Closed-cycle configuration



Understanding spray dryer capacity

How to characterise the size of a spray dryer

The size of a spray dryer is best described by the flow rate of process gas that the plant is intended to handle. As an example, take 1250 kg/h of process gas. The gas disperser in the top of the drying chamber is designed at this flow rate to supply a uniform and efficient mix of hot gas and the feed droplets produced by the atomizing device (e.g. pressure nozzle). Similarly, the cyclone design functions to efficiently separate particles from the gas at the 1250 kg/h flow rate. The gas flow also determines the filter area required in the bag filter and the diameter of the ducts.

In reality a spray dryer does not “produce” powder but rather it evaporates liquid – to create dry particles. The temperature of the process gas going into the drying chamber is the driving force – and the larger the difference between inlet and outlet temperature, the more energy consumed by evaporation. Water requires more energy to evaporate than for example ethanol. Therefore, the curves on the next page illustrate evaporation rates of four different solvents at an outlet temperature typically used for each solvent.

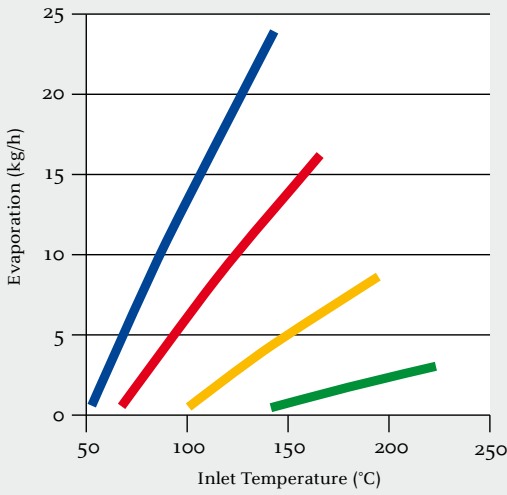
When you know the evaporation rate and the solids concentration of your feed liquid, you can calculate the powder production rate. To increase the powder rate, first look if the solids concentration in the feed can be increased – and then optimise process temperatures.

Having selected a specific size spray dryer, such as the GEA Niro PHARMA^{SD}™ type PSD-4, you can use the curves to evaluate the capacity. When a water-based feed with 20 % solids is dried at inlet/outlet temperatures of 200 °C/90 °C, then approximately 50 kg of water (= 80 %) is evaporated per hour and 12.5 kg/ of powder is produced.



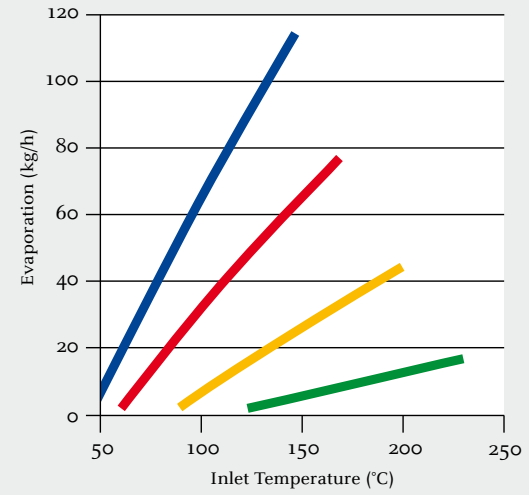
PHARMASD™ type PSD-1

Nominal drying gas rate: 80 kg/h



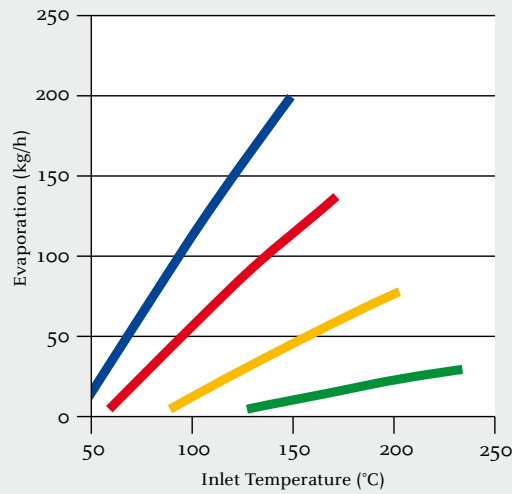
PHARMASD™ type PSD-2

Nominal drying gas rate: 360 kg/h



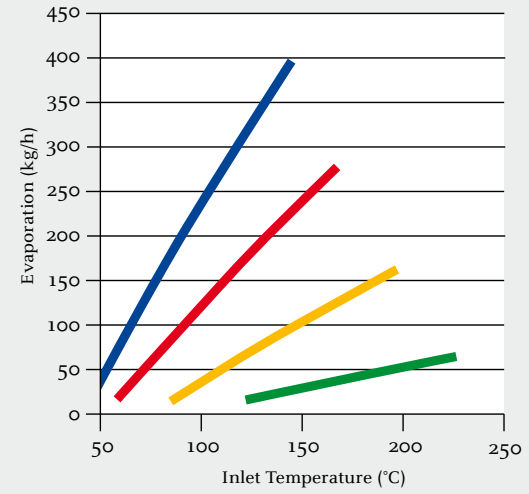
PHARMASD™ type PSD-3

Nominal drying gas rate: 630 kg/h



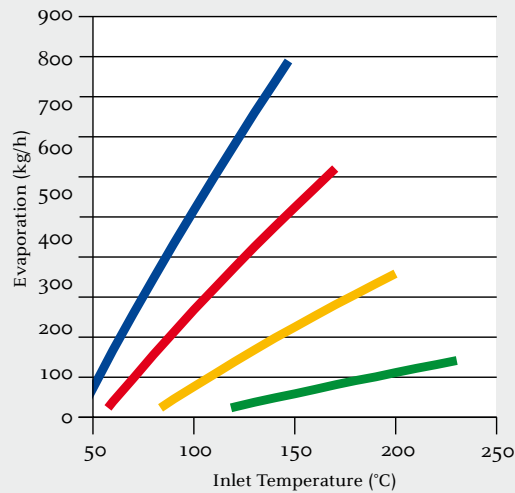
PHARMASD™ type PSD-4

Nominal drying gas rate: 1250 kg/h



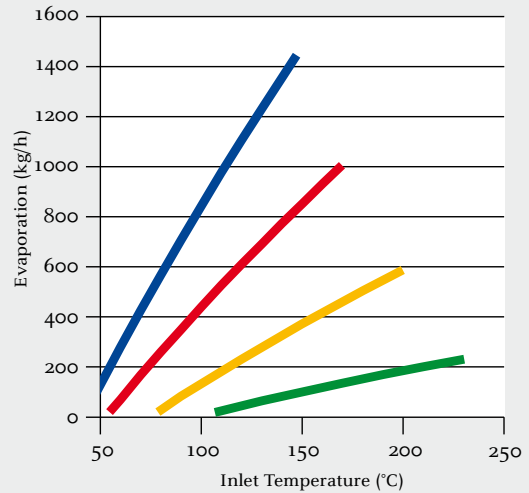
PHARMASD™ type PSD-5

Nominal drying gas rate: 2500 kg/h



PHARMASD™ type PSD-6

Nominal drying gas rate: 5000 kg/h



- Methylene chloride evaporation rate at outlet gas temperature 40 °C
- Acetone evaporation rate at outlet gas temperature 50 °C
- Ethanol evaporation rate at outlet gas temperature 70 °C
- Water evaporation rate at outlet gas temperature 90 °C

Cleaning solutions to suit your process



Custom-designed GEA Niro PHARMASD™ type PSD-4 chamber roof with gas disperser and top of bag filter.

Plant hygiene is one of the first priorities when dealing with healthcare products. GEA Process Engineering offers a full range of cleaning options, with components designed to support specific cleaning methods. The choice of cleaning method has important implications for plant design as well as for control system functionality.

For some products, a hose is sufficient for cleaning the drying chamber while other products require that the atomization device is replaced with an orbital cleaner. Plants dedicated to one product may benefit from an automatic and validated cleaning procedure where cleaning with minimal disassembly calls for special components such as a swing cone access to the chamber and automatic CIP (Clean-In-Place) nozzles.

In small spray drying plants like PharmaSD™ type PSD-1 and PSD-2, clamp connections join ducts and main components, making dismounting and manual cleaning easy. In larger plants with wider ducts, different types of cleaning nozzles can be mounted.

For optimal efficiency, the spray dryer is divided into several cleaning zones and run by a control system with minimal manual operation. Fully automated CIP sequences include: rinse, wash with caustic detergent, rinse, wash with acid detergent and final rinse with purified water.



The GEA Tuchenhausen orbital cleaner adds physical impact to the cleaning.



GMP suite with a GEA Niro PHARMASD™ type PSD-4 spray dryer in chamber with swing cone.

Process control, potent drugs and aseptic production

Process control

In standard GEA Niro PHARMA^{SD}™ plants, the control system can be simple, but of course support GMP guidelines. Process data and alarms can be logged and an audit trail is available. As the plant increases in complexity, or pre-defined recipes or batch reports are required, then GEA Process Engineering offers control systems to match.

Potent drugs

GEA Process Engineering also applies leading technologies and expertise for enabling the possibility of containment. Plants are run in slightly negative pressure and employ GEA Buck split valve technology. GEA Process Engineering experts work closely with customers to conduct detailed risk assessments and determine the optimal combination of spray dryer, isolator technology, Standard Operating Procedures (SOP's), etc.

Aseptic production

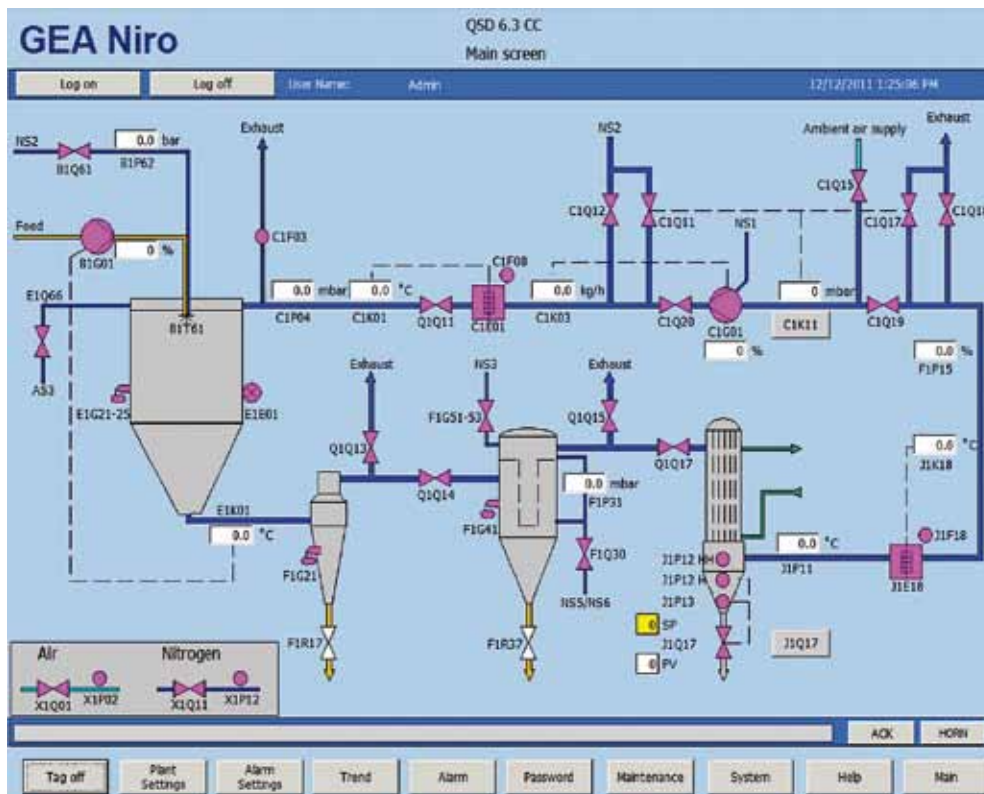
Some products must be produced in plants with low bio-burden or even under aseptic conditions. With years of experience delivering such solutions, GEA Process Engineering recently introduced the next generation of GEA Niro ASEPTIC^{SD}™ Spray Dryers. These plants have an automatic cleaning process involving sterilisation using pure steam. Please contact GEA Process Engineering for more information.



Filter housing for Bag-In-Bag-Out changing of HEPA filter element.



GEA Buck® split valve mounted on cyclone powder outlet.



Control screen of a GEA Niro spray dryer in closed-cycle configuration.

A standard GEA Niro PHARMASD™ Spray Dryer: A cost-effective path to proven results

Based on years of experience with customers of all types (global pharmaceutical companies, producers of API and finished drugs, and small contract manufacture organisations), GEA Process Engineering has developed a proven and robust range of “standard” GEA Niro PHARMASD™ spray dryers.

Despite the level of customer individuality, in many circumstances GEA Process Engineering’s standard PHARMASD™ plants are an ideal and cost-effective solution. With no or only minor modifications, the process set-up and the controls software can be configured. This results in significant savings in engineering hours, also when it comes to qualification activities like the Factory Acceptance Test (FAT), Site Acceptance Test (SAT) and Installation/Operation Qualification (IQ/OQ).

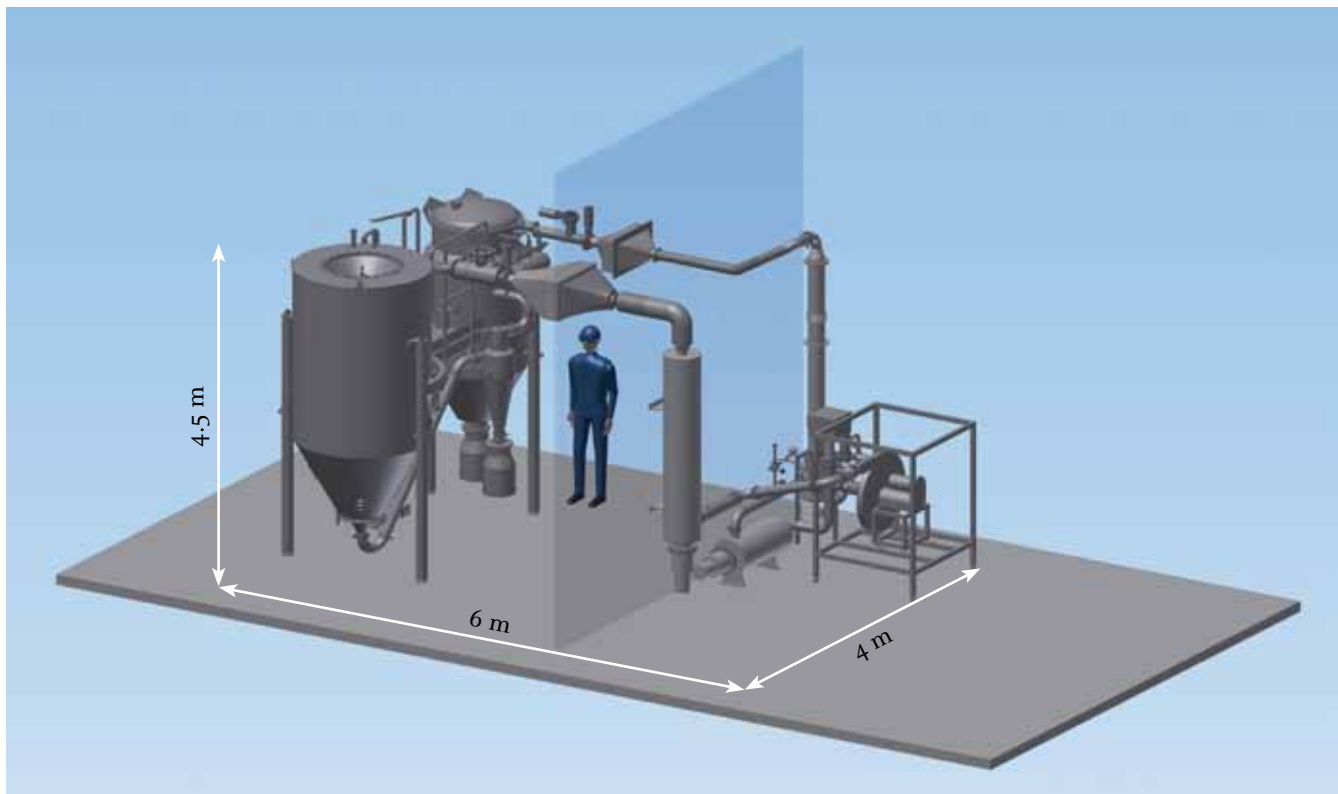
Of course, choosing a standard PHARMASD™ plant is more than just a financial decision. Your product’s Critical Quality Attributes (CQA) are of paramount importance. GEA Niro’s Test Centre provides total assurance, enabling your drug delivery scientists to spray dry and test powder samples before the purchase decision is taken. Your QA people are also welcome to audit our quality system and observe how GEA Process Engineering’s qualification protocols and test documentation fulfil required standards.



GEA Niro PHARMASD™ type PSD-1 spray dryer for closed-cycle operation with solvent-based feeds. Nominal drying gas rate: 80 kg/h.



GEA Niro PHARMASD™ type PSD-2 spray dryer. Nominal drying gas rate: 360 kg/h.



Standard GEA Niro PHARMASD™ spray dryer type PSD-2 in closed-cycle configuration.

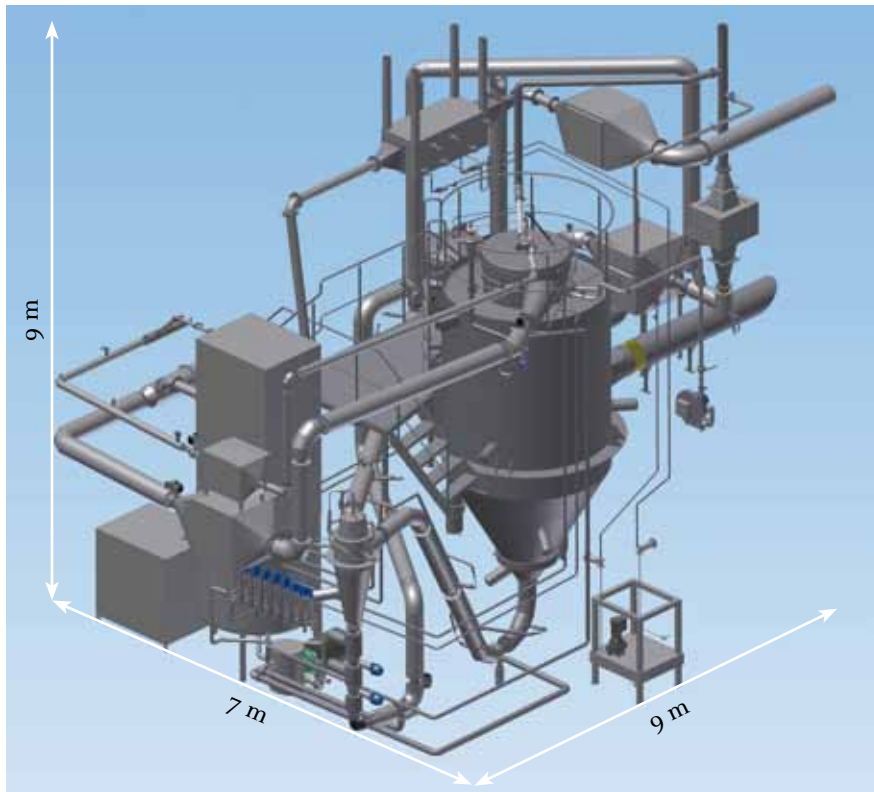
Customised solutions for specific needs

GEA Process Engineering's PHARMASD™ platform allows a high degree of customisation to adapt to specific needs and we offer a range of options, components and add-ons to meet unique demands.

Our GEA Niro PHARMASD™ Spray Dryer, for example, has been customised to produce powder with low bio-burden for terminal sterilisation. In other cases, the physical properties of the API or the CQA are so challenging that custom designs arise from test work.

Especially in the case of larger spray dryers, installations need to be adapted specifically to your site. Integrating feed preparation systems, powder handling equipment and Clean-In-Place (CIP) liquid skids is carried out by exchanging 3-D drawings with your project group.

Large production facilities may use standardised instrumentation from a specific manufacturer, or the control system may have to be integrated with your SCADA system. GEA Process Engineering engineers are familiar with such requirements and work in close cooperation with your specialists to design optimal solutions.



Custom-designed GEA Niro PHARMASD™ type PSD-3 with explosion venting panels, automatic Clean-In-Place system, and heat recovery.



Custom-designed GEA Niro PHARMASD™ type PSD-1 spray dryer in clean room.



Powder collection in clean room, GEA Niro PHARMASD™ type PSD-4.

A sure path to healthy business

At GEA Process Engineering we know there is a lot more to formulating drugs than having the right equipment. That is why we have never considered ourselves an equipment supplier but rather a process development partner. We can help with all aspects of investigating how spray drying could enhance your drug formulation.

Our capabilities span everything from reviewing particle characteristics right through to process development, producing clinical trial materials and large-scale test production. Customers gain a secure outcome, clinical trial materials and reduced time to market.

Beyond steel

Apart from hardware, collaborating with GEA Process Engineering also gives you access to the greatest concentration of industrial drying experts in the world. You'll find analysts versed in assessing and refining particle design; process engineers practised in overcoming the difficulties of scaling to commercial production; and people familiar with the intricacies of regulatory procedures.

The world's most advanced GMP facility for spray drying

GEA Process Engineering's Pharmaceutical Spray Drying facility is a unique GMP test and production facility, certified for the production of clinical trial materials. The facility complies with the EU's requirements for the production of Investigational Medicinal Products (IMP) and is exclusively there to aid you in drug development projects.

Product development process

Spray drying projects begin by listening to a customer's product aspirations. Once we understand these objectives we can recommend a process for achieving the desired result.

Bench analysis and trials

In the early drug development phase when only very limited amounts of material are available, single droplet drying is ideal for testing the feasibility of spray drying and addressing basic formulation questions. With GEA Niro's DRYING KINETICS ANALYZER™ and spray drying expertise, only a few mL of feed material are needed to examine the morphology and establish the basic spray drying process.



Small-scale pilot tests

The next step involves optimising the process and creating samples for technical analysis. With spray dryers available in several sizes, we can produce samples in a capacity of a few grams/hour up to several kilos/hour - amounts sufficient for both technical analyses and product development.





The facility allows you to carry out all essential product development work, while limiting the need for upfront investments.

Leaving nothing to chance

Offering both micro-plants and full-size spray drying plants, the GEA Niro Test Centre makes it easy to scale-up projects to commercial proportions, and our proprietary know-how and unparalleled facilities reduce development time at every step. Being able to run full-scale tests allows you to train staff and qualify processes in parallel with the commissioning of your own commercial production unit. This substantially compresses the time used in the switch to commercial production.

Scale-up

Before turning to GMP testing, we make final process adjustments by running large-scale plants at a similar capacity as the final production plant.



Toxicology studies, clinical trial materials and GMP manufacturing

Our GMP spray drying facility is available for the production of materials for customers' own stability and safety/toxicology studies, clinical trial materials and commercial purposes. The facility is one of the most advanced in the world and is equipped with two GEA Niro Pharmaceutical Spray Dryers: a PHARMASD™ type PSD-1 for production in small quantities and a PHARMASD™ type PSD-4 for large-scale production.



Commercial production

Once you are confident in the quality of the final product and have all the process and product documentation you need, we move ahead with installing a facility at your site.





Excellence

Passion

Integrity

Responsibility

GEA-versity

GEA Group is a global mechanical 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.



GEA Process Engineering

GEA Niro

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