



# GEA Niro Pharmaceutical Spray Dryers

A unique union of proven technology  
and customised solutions



GEA Process Engineering  
**GEA Niro**

bringing powder to life™



*From GEA Niro Pharma Test Station in Copenhagen:  
GMP suite with a PSD-4 spray dryer in closed-cycle mode*

# Process expertise and experience

For 75 years, GEA Niro has supplied drying plants for powders to the pharmaceutical industry worldwide. This includes small-capacity dryers designed for R & D as well as industrial-size plants for continuous 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 more than twenty thousand tests performed, we have established an extensive knowledge base related to the needs of the pharmaceutical and biopharmaceutical manufacturing industries.

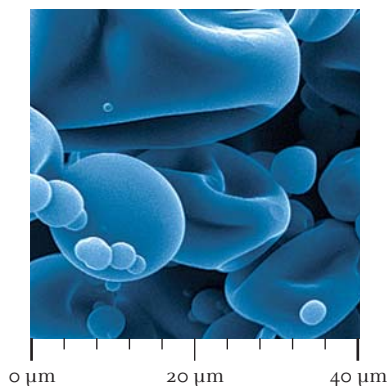
## **Delivering the right solutions**

Every GEA Niro plant begins with the desire to develop a product that will succeed in the market. In GEA Niro, you will find a partner who will assist you in meeting that goal. Our expertise includes technologies for processing Active Pharmaceutical Ingredients (API) using spray drying, agglomeration, encapsulation, and spray congealing as well as drying of final drug formulations.



*From GEA Niro Pharma Test Station in Copenhagen:  
GMP suite with a PSD-1 spray dryer in closed-cycle mode*

# Five ways spray drying can help you commercialise discoveries



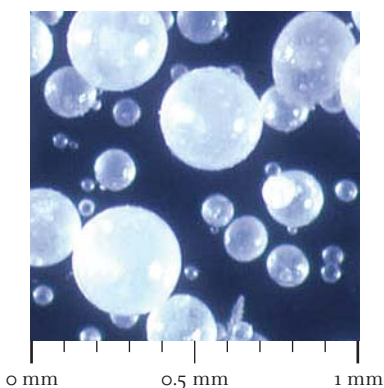
## 1. Increased bioavailability

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

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

An interesting technique for the improvement of the dissolution rate is by the creation of nanoparticles which are isolated and recovered by the spray drying process.

By enhancing the dissolution rate in this way, spray drying has the potential to make possible new treatments that are currently not viable due to low bioavailability.

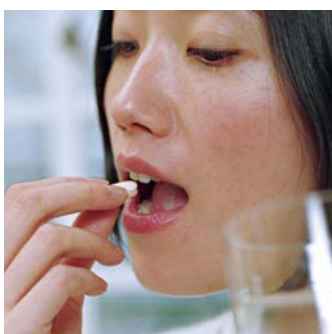


## 2. Modified release or taste masking

Encapsulation offers drug developers a number of commercial and medical advantages. E.g., it can be used for the sustained release of some antibiotics reducing dosage requirements. By preventing drug concentration peaks, encapsulation is also an effective way to treat chronic illness – e.g., cancer or AIDS – with reduced side effects. The technique is also widely employed for taste masking and the physical protection of the API.

Spray drying makes it possible to engineer particles in order 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.

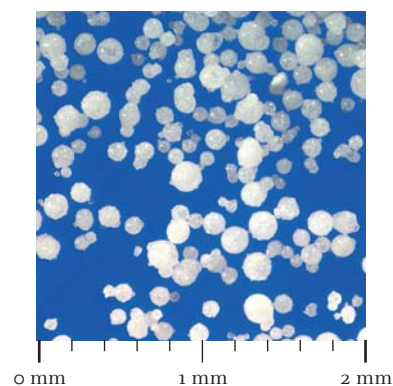
An interesting alternative approach is spray congealing, where the API is melted or mixed with molten excipient and the powder particles produced by atomization and cooling.



### 3. Aseptic production

Aseptic spray drying offers a number of advantages over traditional methods of aseptic drying such as lyophilisation. More specifically, by allowing precise control of the drying process, spray drying gives you far greater command over the shape and morphology of the final product. What's more, with lower running and capital costs, you attain these advantages while reducing overheads.

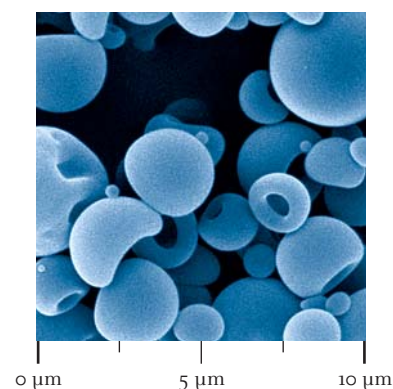
Production of dry sterile dosage forms often involves mixing of the API with one or more excipients. To achieve a homogeneous mixture, the particle size distribution of the excipient(s) must match that of the API. In a one-step-operation, spray drying can turn a sterile solution into sterile particles of the required size with no risk of introducing impurities - a well-known problem if milling is used.



### 4. Products for inhalation

Inhalation is a pain-free and self-administrable delivery method and for these reasons is preferred by patients and medical professionals, whenever applicable. Yet 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 Niro has developed highly specialised spray drying nozzles that give you far greater particle engineering capabilities, even at a large scale, making it possible to accurately manipulate aerodynamic particle size and flow properties.



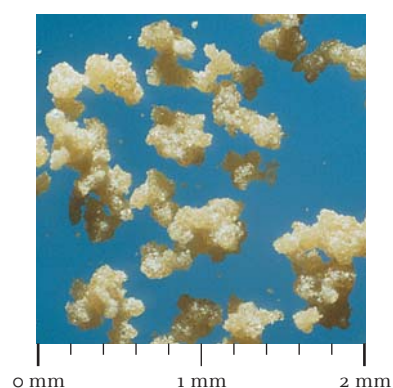
Consequently our technology makes it easier than ever before to efficiently produce therapies in the form of free-flowing particles of a small aerodynamic size, suitable for inhalation.

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

### 5. Direct compressibility

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

With the Fluidized Spray Dryer – FSD™ concept, the granulation step can be made an integral part of the continuous drying process - a technique pioneered by GEA Niro. The FSD™ technology can also be used to achieve a low residual volatiles content in the final spray dried powder. This not only results in a more streamlined, efficient production process, but also reduces cost.



# Five things you might not know about spray drying



*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. (Patent pending)*



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

## **1. Spray drying is suitable for heat sensitive materials**

Spray drying is already used for the processing of heat sensitive materials (e.g. proteins, peptides and polymers with low  $T_g$  temperatures) on an industrial scale. Evaporation from the spray droplets starts immediately after contact with the hot process gas. Since the thermal energy is consumed by evaporation, the droplet temperature is kept at a level where no harm is caused to the product.

## **2. Spray drying turns liquid into particles within seconds**

The large surface of the droplets provides near instantaneous evaporation, making it possible to produce particles with a crystalline or amorphous structure. The particle morphology is determined by the operating parameters and excipients added to the feed stock.

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

GEA Niro has been producing industrial scale spray drying plants for well over half a century. Our process know-how, products and exceptional facilities put us in a unique position to advise and demonstrate how products and processes will behave on a large scale.

## **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 the batch. Information for the batch record can be monitored or logged, depending on the system selected.

## **5. Spray drying can be effectively validated**

GEA Niro has extensive experience of supplying 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.

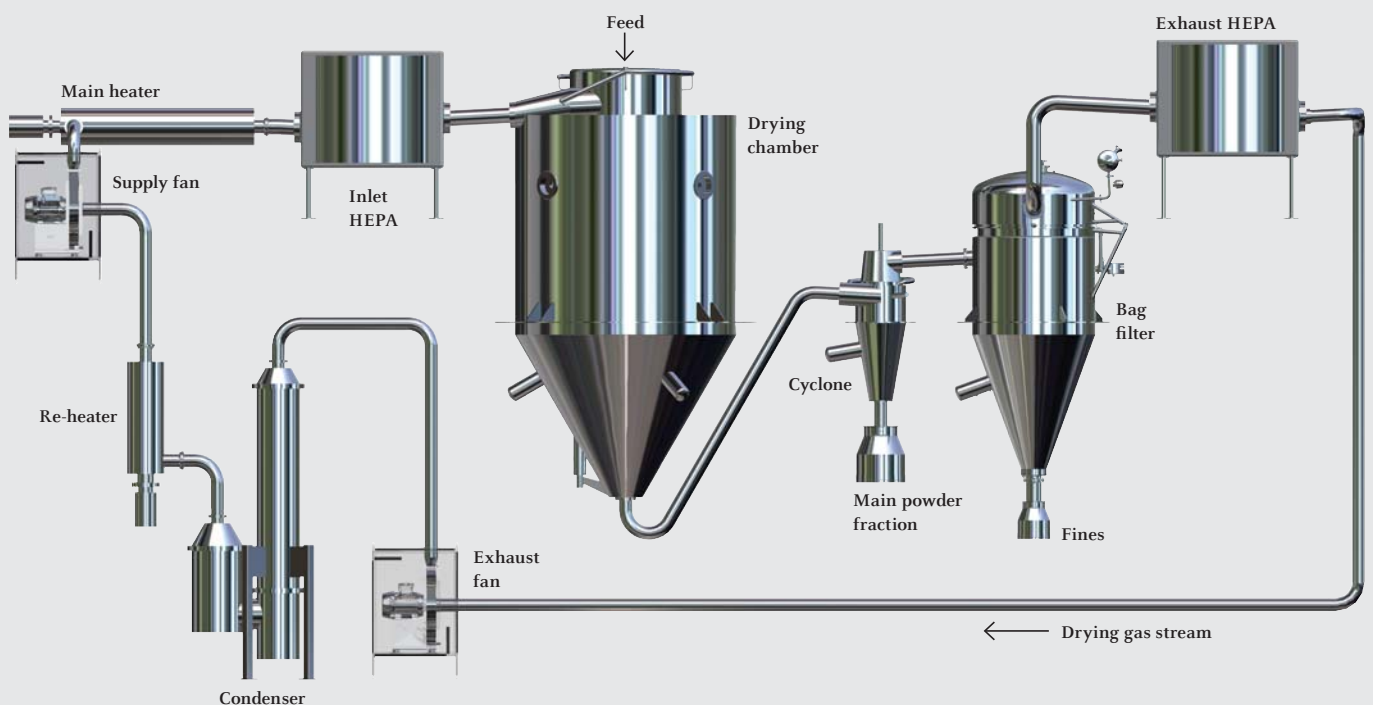
# The spray drying process

Spray drying is a very fast method of drying due to the very large surface area created by the atomization of the liquid feed and high heat transfer coefficients generated. The short drying time, and consequently fast stabilisation of feed material at moderate temperatures, means spray drying is also suitable for heat-sensitive materials.

As a technique, spray drying consists of four 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:** Hot process gas (air or nitrogen) is brought into contact with the atomized feed guided by a gas disperser, and evaporation begins. The balance between temperature, flow rate and droplet size controls the drying process.
- c. **Particle formation:** As the liquid rapidly evaporates from the droplet surface, a solid particle forms and falls to the bottom of the drying chamber.
- d. **Recovery:** The powder is recovered from the exhaust gas using a cyclone or a bag filter. The whole process generally takes no more than a few seconds.

## Closed-cycle spray drying system



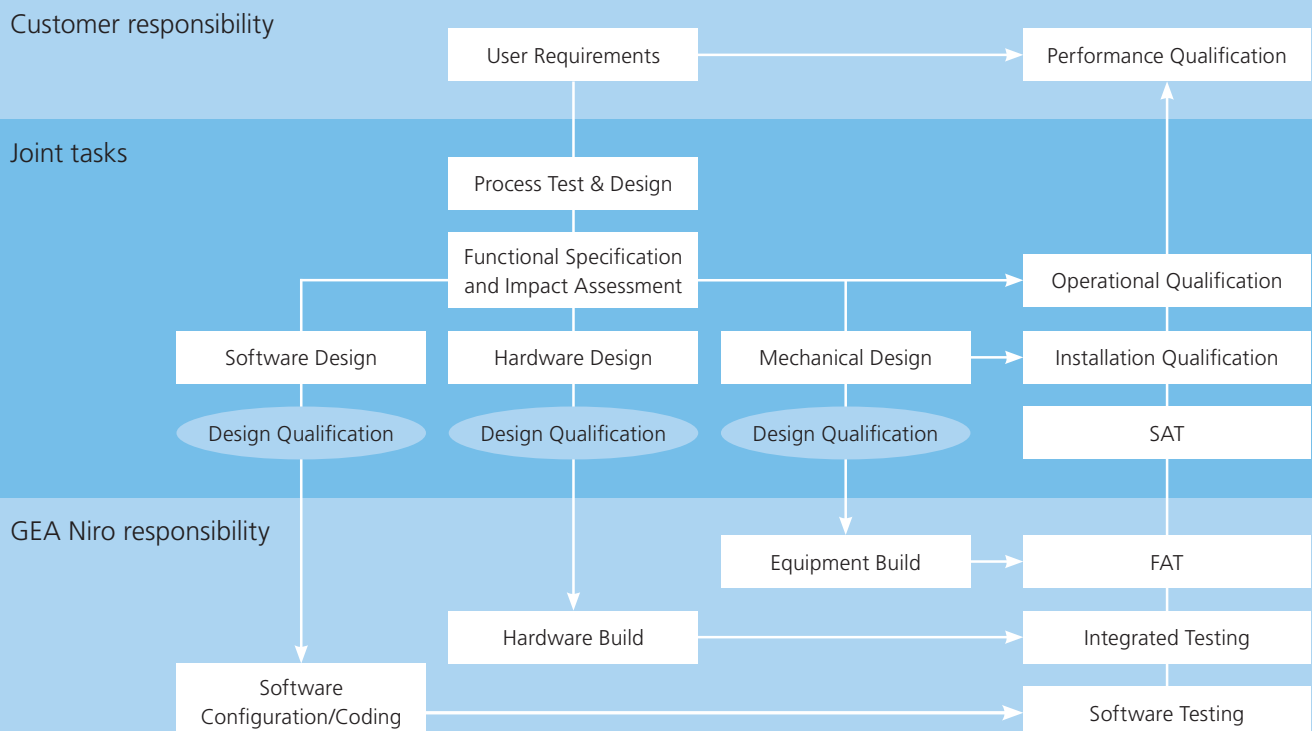
# The complete partnership

## Working with you...

Entering a partnership with GEA Niro 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 qualified 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 GEA Niro.



# Meeting every requirement

GEA Niro has developed a series of spray dryers to meet the high requirements of the pharmaceutical industry.

## Tailor-made solutions

The philosophy behind the design is that a combination of standardised modules are built together in order to meet the requirement for a specific duty. Therefore, dryers of equal capacity may be completely different with respect to design, configuration and physical size. Specific requirements for choice of materials, surface treatment, containment or other features are included in the customized design. Each module, indeed each system component, must meet the strictest requirements and regulatory standards around the world.

## Spray drying organic solvents

The use of solvents when preparing pharmaceutical ingredients poses a challenge in the drying process and has resulted in the use of nitrogen as a drying gas. Our spray dryers are configured for drying of compounds that are based on acetone, methylene chloride, ethanol, and other organic solvents. The drying parameters and capacity vary greatly, depending on the solvent used, as shown in the tables on page 12-13.



*PSD-1 drying chamber, cyclone and bag filter.  
Nominal drying gas rate: 80 kg/h*



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



*QSD-o.8 spray dryer for closed-cycle  
operation with solvent-based feeds.  
Normal gas drying rate: 80 kg/h*

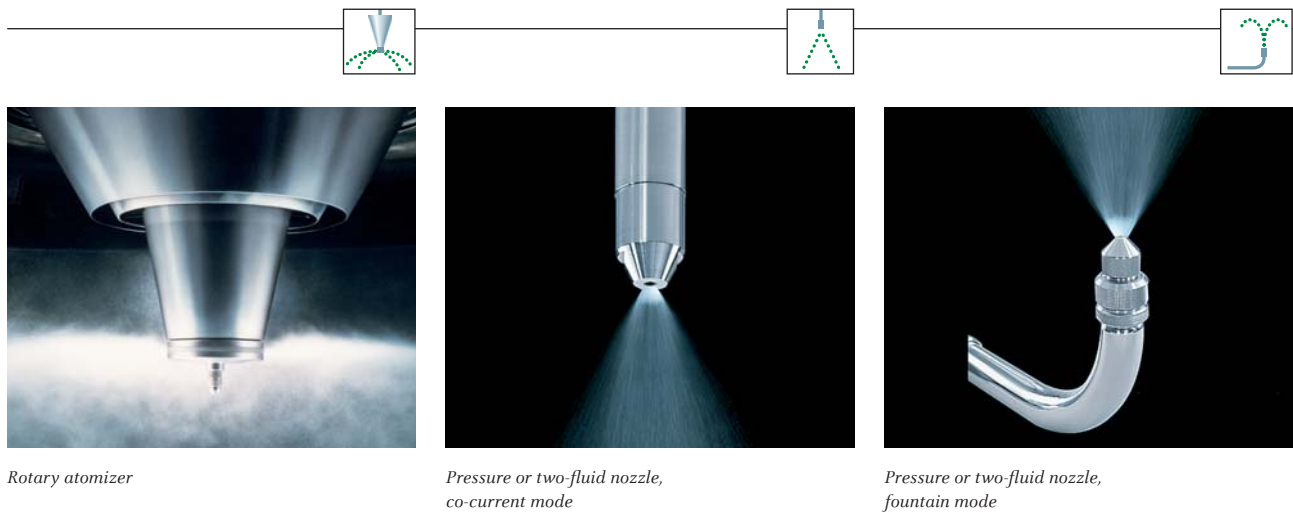
# Standardised customisation

## Atomization and powder discharge

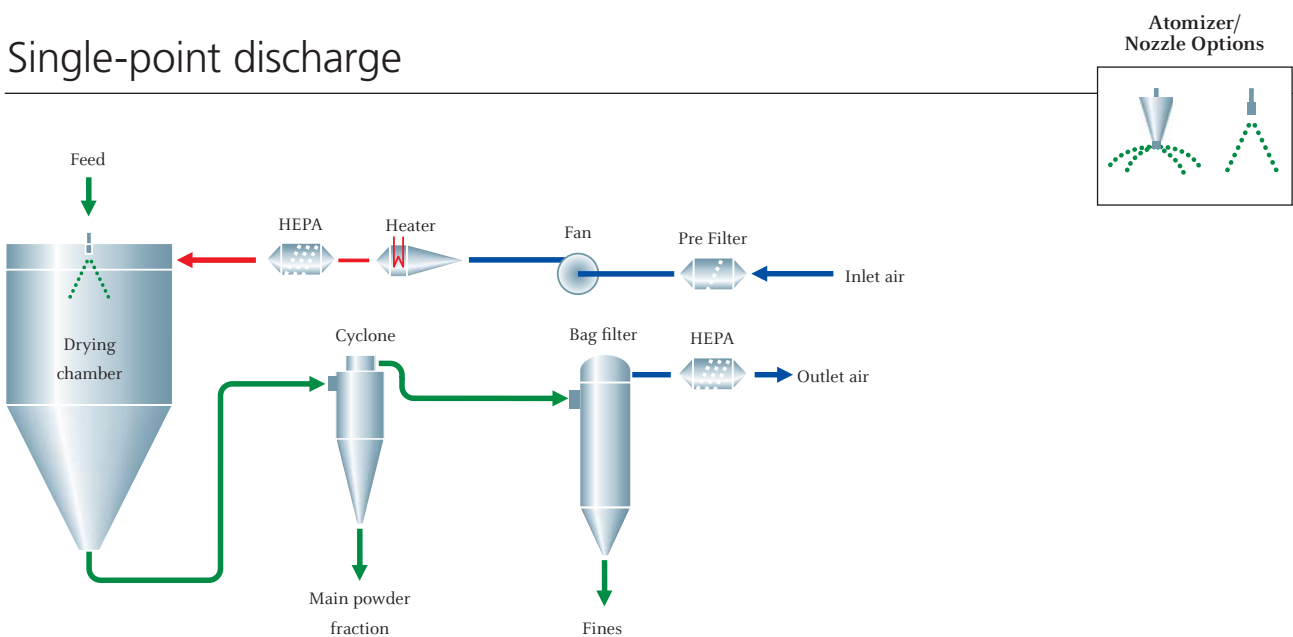
One of the most important choices in a plant configuration is choosing the right atomization and powder discharge method. We offer a wide range of solutions, as illustrated.

For operation with feeds based on flammable solvents or powders subject to explosion risk, dedicated designs are available.

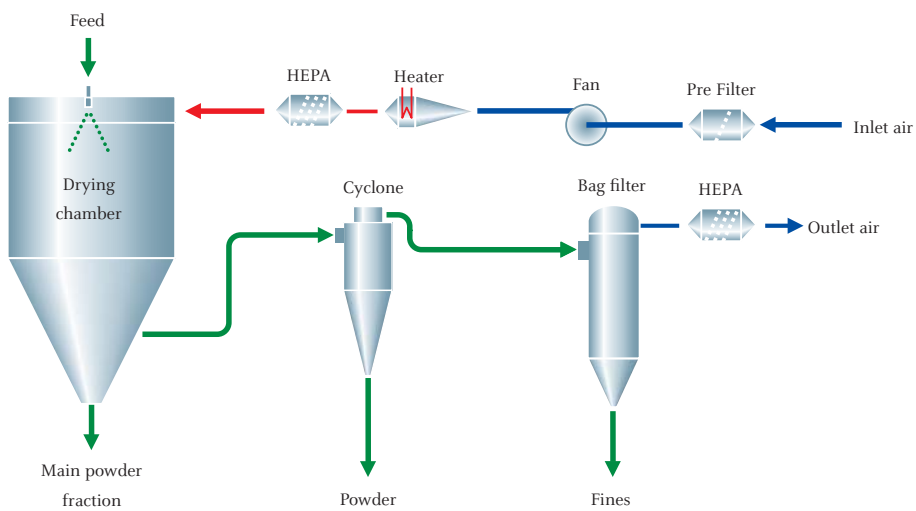
## Atomizer/Nozzle options



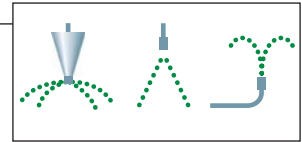
## Single-point discharge



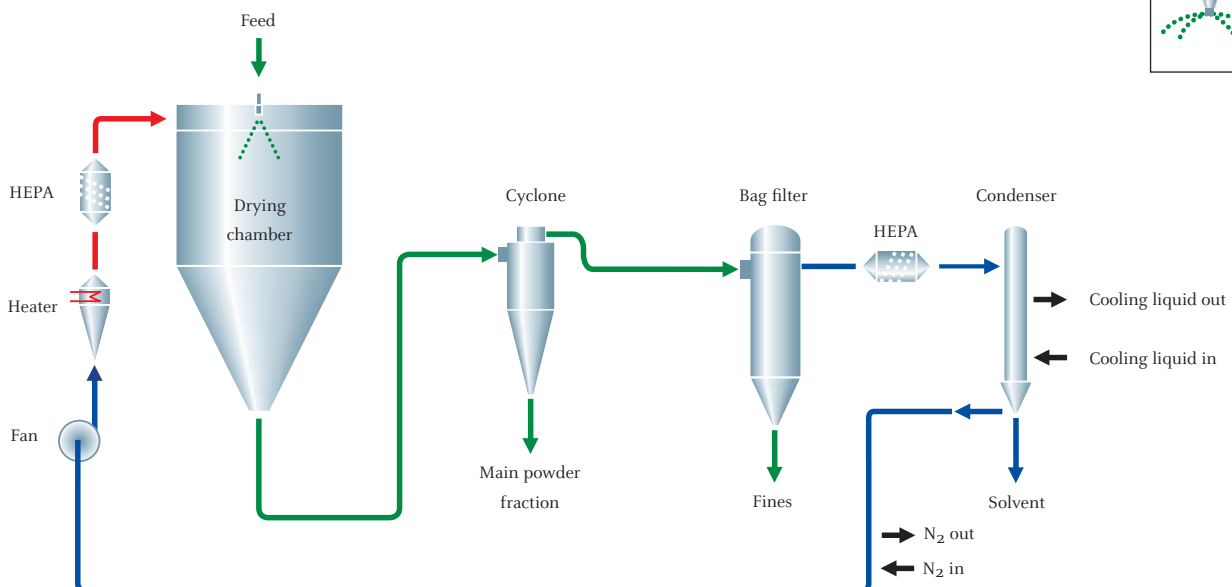
## Two-point discharge



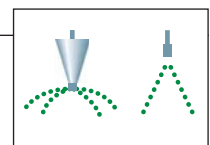
Atomizer/  
Nozzle Options



## Closed-cycle design



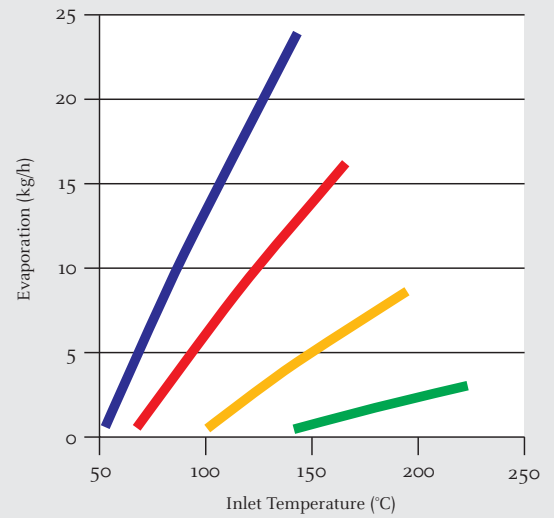
Atomizer/  
Nozzle Options



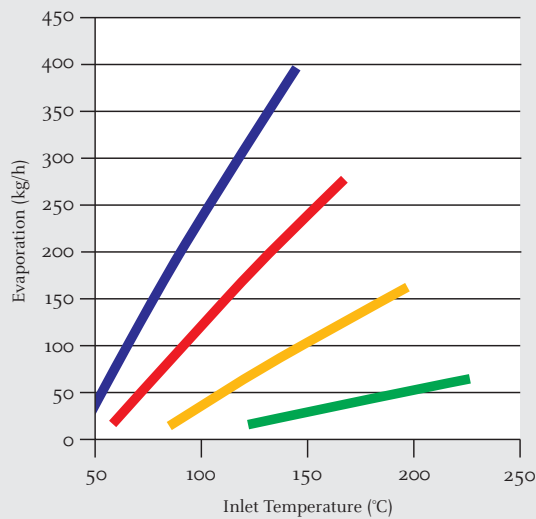
# The PHARMA<sup>SD</sup>™ series

- █ 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

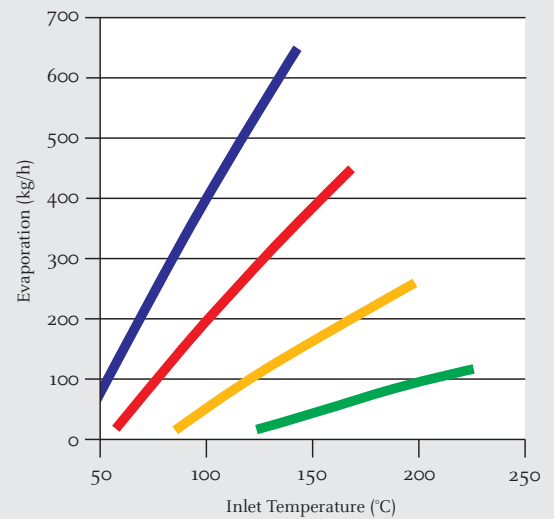
**PSD-1 co-current atomization**  
Nominal drying gas rate: 80 kg/h



**PSD-4 co-current atomization**  
Nominal drying gas rate: 1250 kg/h

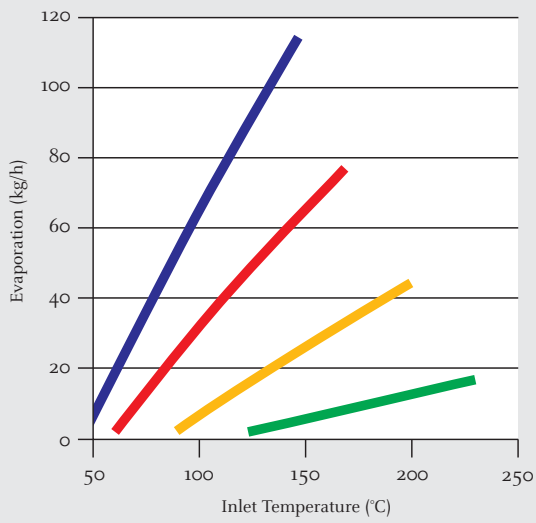


**PSD-5 co-current atomization**  
Nominal drying gas rate: 2000 kg/h



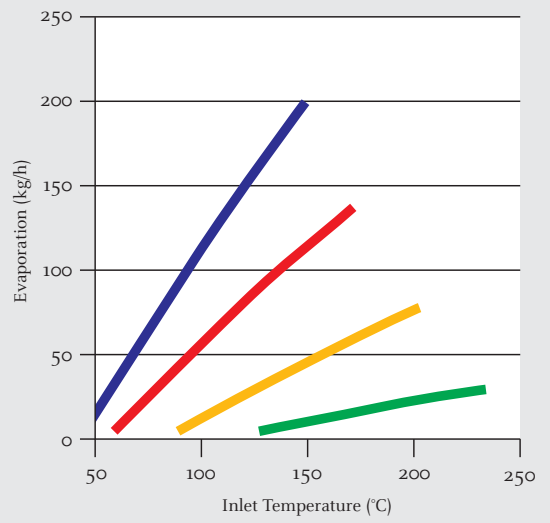
### PSD-2 co-current atomization

Nominal drying gas rate: 360 kg/h



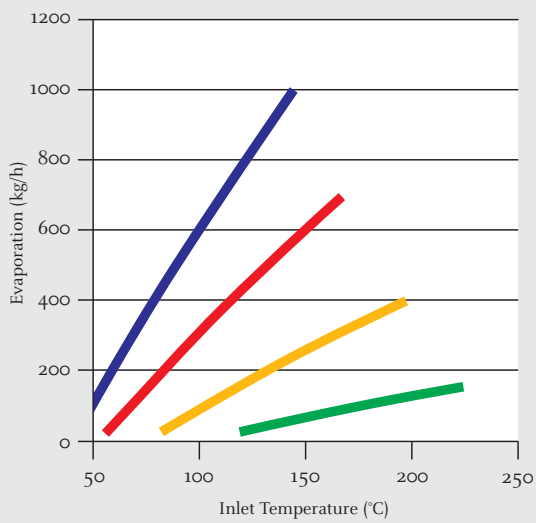
### PSD-3 co-current atomization

Nominal drying gas rate: 630 kg/h



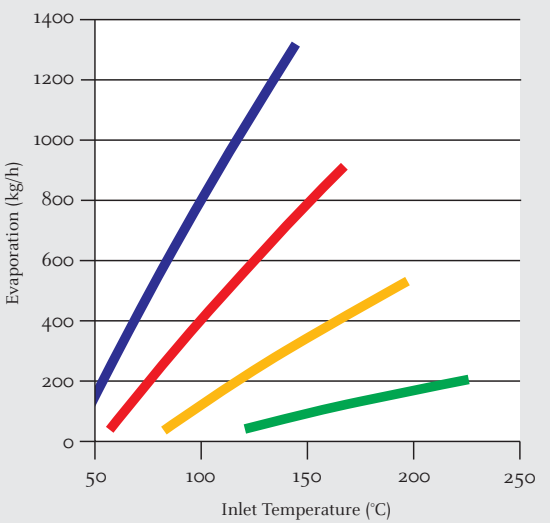
### PSD-6 co-current atomization

Nominal drying gas rate: 3150 kg/h



### PSD-7 co-current atomization

Nominal drying gas rate: 4000 kg/h



# A sure path to healthy business

At GEA Niro we know there is a lot more to formulating therapies 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 trials material and large-scale test production. Central to our ability to deliver this level of service is GEA Niro's unique Test Center also including a GMP certified Pharma Test Station. This facility provides customers with security of outcome, clinical trials material and reduced time to market.

## Beyond steel

Apart from hardware, collaborating with GEA Niro 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 drug development cycle



### Pilot tests

*Small-scale tests in our pilot plants provide proof of concept and highlight areas that require further attention. At this initial stage only small amounts of the product are needed.*

### Product development

*Spray drying projects begin with listening to a customer's product aspirations. We can then suggest a process for achieving the desired result.*



### Analysis

*In our fully equipped onsite lab, qualified personnel are available to verify the results of pilot studies, review powder and particle characteristics and suggest modifications to the process.*



**The world's most advanced GMP test station for spray drying**

GEA Niro's international Pharma Test Station is a unique GMP facility, certified for the production of Clinical Trials Material. The station accords with the EU's requirements for the production of Investigational Medicinal Products (IMP) and is exclusively there to aid you in drug development projects.

The concept behind our facility is to allow you to carry out all essential product development work, while limiting the need for upfront investment in spray drying equipment.

**Leaving nothing to chance**

The test facilities are the ideal setting for defining and refining products, delivery methods and processes. Offering both micro-plants and full-size spray drying plants, the Test Center makes it easy to scale-up projects to commercial proportions. And our proprietary know-how and unparalleled facilities reduce development time at every step. Finally, 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 during the final phase of the development cycle.



**Tech transfer**

*The vast range of spray drying equipment available at our site means it's possible to scale up and test products and processes at a commercial production level.*



**Process development and clinical trials**

*Following pilot studies in the general Test Center, our GMP-certified Test Station is the perfect venue to carry out detailed final trials and produce material for toxicity studies and clinical trials.*



**Commercial production**

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



## Central know-how on a global scale

GEA Niro has contracted and installed more than 10,000 plants worldwide

GEA Niro is the world leader in industrial drying, with spray drying, spray cooling/congealing, flash drying, freeze drying, granulation and fluid bed processing as core technologies. GEA Niro is known for delivering solutions that meet customers' exact requirements. With a strong commitment to research and development, pharmaceutical technology centres in Belgium, Denmark, Switzerland, the UK, Singapore, and the 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. The GEA Niro companies are part of GEA Process Engineering.



GEA Process Engineering

### **GEA Niro**

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