



GEA Niro GMP Pharmaceutical Spray Drying facility

Spray drying process development
and contract manufacturing



GEA Process Engineering
GEA Niro

bringing powder to life™



PSD-4 Chamber cone in clean room.

Contract manufacturing services from the world's most advanced spray drying technology centre

The GEA Niro GMP Pharmaceutical Spray Drying facility is part of the GEA Niro Test Centre, the largest and most advanced spray drying technology centre in the world. We have the expertise and capacity to help you in areas crucial to the success of your product:

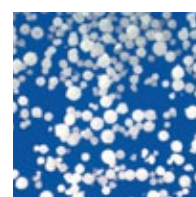
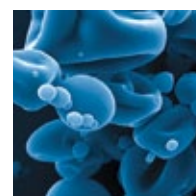
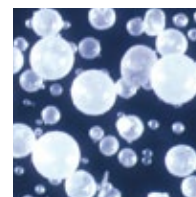
- Spray drying process development
- Contract manufacturing (spray drying) under cGMP conditions

At an early stage, we can conduct test work to help determine if spray drying is the correct technology for your product. If this is the case, we develop the right spray drying process parameters and make test runs and samples, first for technical analyses and – at a later stage – for clinical trials. This can be followed by large-scale cGMP production of clinical trial materials (for Phase II-III trials) or of commercial products. No matter which stage is your starting point, we have the resources to take you further.

The GEA Niro GMP Pharmaceutical Spray Drying facility is approved by the Danish Medicines Agency (according to European Medicines Agency [EMA] regulations) and meets EU requirements for production of Investigational Medicinal Products (IMP). Upon request, approval for production of commercial products can be obtained.

Working with GEA Niro, spray dried products can be developed without any major capital investment before the product is ready to be brought to market.

The GEA Niro GMP Pharmaceutical Spray Drying facility is built according to GMP standards for final drug production with a clean room for powder collection and process control that is 21 CFR part 11 compliant. It includes two fully equipped spray dryers, a PSD-1 and a PSD-4, both in closed-cycle execution.



Rapid, reliable and cost effective process development

Which characteristics are most advantageous for your product? How can a spray drying process be designed to meet your product requirements? Is the process robust? The GEA Niro Spray Drying Technology Centre can help you answer crucial questions about your product at a very early stage, achieve proof of concept quickly and efficiently and move to commercial production.

Meeting the highest industry standards

We currently work with and meet the exact standards of major players at all levels of the pharmaceutical industry: Contract Research Organisations (CROs), Contract Manufacturing Organisations (CMOs), and both large and small integrated pharmaceutical companies. We can apply this experience to provide a high level of service for your product, resulting either in contract production at our facility or assistance with transferring technology and expertise to your own in-house production plant.

Determining the right process for your product

We are able to go from single droplet DRYNETICS™ analysis to large-scale testing and manufacturing. The DRYNETICS™ process enables us to conduct experiments on individual droplets of a feed to determine its actual drying properties and to examine the morphology. The results are then transferred to computational fluid dynamics (CFD) software, making it possible to simulate the correct drying process for your product with unprecedented accuracy.

The GEA Niro Test Centre includes GMP as well as non-GMP facilities and encompasses resources that range from table-top equipment to full-size spray drying technology. To minimise costs, we refine product and process parameters under non-GMP conditions before entering the GMP facilities. All this on the same site.

DRYNETICS™



1. Single droplet experiments

- Temperature
- Size and position
- Adhesion/stickiness
- Morphology

2. Advanced data analysis

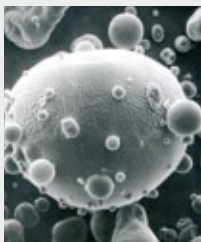
- Drying kinetics
- Density
- Stickiness

A fast route from drug development to commercial production

The GEA Niro Spray Drying Technology Centre includes GMP as well as non-GMP facilities. These allow you to go quickly and efficiently from the early stages of product development, where only a few millilitres of liquid product are available, to the final phases of process refinement and commercial production.

non-GMP

Expertise at every stage



Scanning electron microscope (SEM) picture of a spray dried particle.

Bench analysis and trials

In the early drug development phase, when only very limited amount of material is available, single droplet drying is ideal for testing the feasibility of spray drying and to address basic formulation questions. With GEA Niro's DRYNETICS™ and spray drying expertise, only a few ml of feed material is needed to examine the morphology and to establish the basic spray drying process parameters.



Small-scale pilot tests

A step further, we can develop the optimum spray drying process and make samples for technical analysis. With spray dryers in several sizes available, we can produce samples in a capacity of a few grams/hour up to several kilos/hour - sufficient for technical analyses and product development.

The SDMicro™ spray dryer is placed in an isolator for operator safety.



PSD-4 Chamber roof with gas disperser and top of bag filter.



PSD-4 raw material reception.

GMP



Scale-up

Before turning to GMP testing, we optimise the process by running on large-scale plants that can have the same capacity as the final production plant.

The closed-cycle 12.5 plant is equal in capacity and dimensions to the PSD-4 spray dryer.



Toxicology studies, clinical trial materials and GMP manufacturing

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

Feed preparation on the PSD-1 spray dryer.



Clear understanding and communication

Decades of experience with developing spray drying processes have given us a good understanding of our customers R&D processes, timing, critical parameters, etc. At the start of a project, we sign a confidentiality agreement, and work with you to define project and production expectations, milestones and goals and spell out our individual and joint responsibilities. Basic documentation is established for the development phases and a commercial production agreement is finalised. Formal protocols are prepared and approved by both parties before any development work or production begins.





PSD-4 chamber and HVAC ducts.



PSD-4 CIP (Clean in Place) tanks.

Case 1: Saving time for a large pharmaceutical company

The GEA Niro GMP Pharmaceutical Spray Drying facility recently worked with a large pharmaceutical company to develop a spray drying process for a promising product. This first stage required a few weeks of work. After that, we:

- Scaled up the process and conducted a large-scale series of boundary and process robustness tests to establish the limits for the spray drying process. This took a few months to complete.
- Completed technology transfer of the process to the GMP facility, which required a few weeks.
- Accomplished production of material for Phase II and III clinical trials, which took about two years. In the meantime, the customer purchased and installed industrial-scale spray dryers for commercial production.

Our customer not only saved a lot of time during this process, but was also able to delay investment in production equipment until the probability for product success was very high.

Case 2: Working together with a Contract Research Organisation

In a recent project for a CRO, the GEA Niro GMP Pharmaceutical Spray Drying facility participated in the development of a spray drying process. The first task was to use spray drying to screen a number of different formulations based on the same active ingredient. This required a few weeks. After that, we:

- Optimised the spray drying process for the best formulation based on initial trials
- Completed technology transfer to GMP plants
- Produced material for Phase II and III clinical trials



Powder collection in clean room, PSD-4.

Industry-leading experience and expertise

GEA Niro has refined spray drying technology to match pharmaceutical industry requirements. As the world's leading supplier of spray dryers, with more than 75 years experience in spray drying, GEA Niro is particularly qualified to handle your pharmaceutical contract manufacturing needs.

Pharmaceutical spray drying offers a number of unique advantages, including:

- Increased bioavailability
- Controlled release or taste masking
- Production of fine powders for inhalation or other applications
- Production can be conducted under aseptic conditions
- Production of APIs and excipients as well as of solid dosage formulations of final drugs

PSD-4 feed preparation.





PSD-1 spray dryer in clean room.



PSD-4 chamber cone in clean room.

PHARMASD™, PSD-1

Plant configuration

- Main components: Chamber, cyclone, bag filter, HEPA filters, condenser, electrical heaters
- Nitrogen as drying gas
- Closed-cycle loop
- Powder collection under cyclone and/or bag filter. Bag filter for collecting fines
- Atomization methods:
 - Two-fluid nozzle, co-current

Feed

- Mixing of various solvents possible
- Dosing and mixing of various raw materials possible
- Filtration of feed possible – also sterile filtration

Solvents

- Water
- Ethanol
- Methanol
- Isopropyl alcohol
- Acetone
- Methylene chloride
- Ethyl acetate

Operating parameters

Inlet temperature	up to 180 °C
Outlet temperature	up to 150 °C
Condenser temperature	down to -18 °C
Feed rate	up to 10 kg/h (depending on solvent type)
Feed temperature	5 °C to 80 °C
Two-fluid nozzle, atomization gas temperature	18 °C to 100 °C

CIP

- CIP (Clean in Place) liquid temperature: Up to 80 °C

PHARMASD™, PSD-4

Plant configuration

- Main components: Chamber, cyclone, bag filter, HEPA filters, condenser, electrical heater
- Nitrogen as drying gas
- Closed-cycle loop
- Powder collection under cyclone and/or bag filter. Bag filter for collecting fines
- Atomization methods:
 - Pressure nozzle, co-current
 - Two-fluid nozzle, co-current

Feed

- Mixing of various solvents possible
- Dosing and mixing of various raw materials possible
- Filtration of feed possible – also sterile filtration

Solvents

- Water
- Ethanol
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- Isopropyl alcohol
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Operating parameters

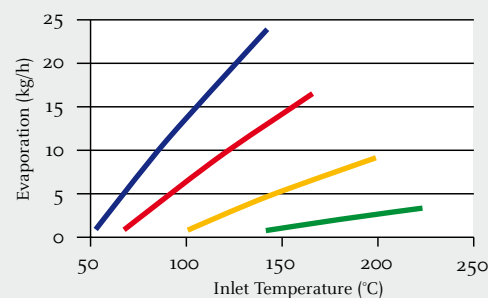
Inlet temperature	up to 220 °C
Outlet temperature	up to 150 °C
Condenser temperature	down to -18 °C
Feed rate	25 kg/h to 250 kg/h (depending on solvent type)
Feed temperature	5 °C to 80 °C
Pressure nozzle, atomization pressure	10 bar to 100 bar
Two-fluid nozzle, atomization gas temperature	18 °C to 100 °C

CIP

- CIP (Clean in Place) liquid temperature: Up to 80 °C

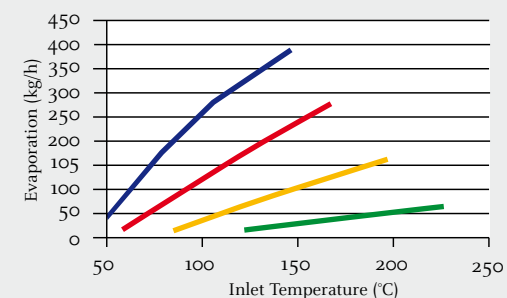
PSD-1 co-current atomization

Nominal drying gas rate: 80 kg/h



PSD-4 co-current atomization

Nominal drying gas rate: 1250 kg/h



■ Methylene Chloride Evaporation Rate at Outlet Gas Temp 40 °C ■ Acetone Evaporation Rate at Outlet Gas Temp 50 °C

■ Ethanol Evaporation Rate at Outlet Gas Temp 70 °C ■ Water Evaporation Rate at Outlet Gas Temp 90 °C



Experience

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

GEA Niro is a world leader in industrial drying, with spray drying, spray cooling/congealing, flash drying, freeze drying, granulation and fluid bed processing as core technologies. Having installed more than 10,000 plants around the globe, GEA Niro is known for delivering solutions that meet customers' exact requirements. The GEA Niro companies are part of GEA Process Engineering.

The GEA Niro GMP Pharmaceutical Spray Drying facility is part of the GEA Niro Test Centre, the largest and most advanced spray drying technology centre in the world. The GEA Niro GMP Pharmaceutical Spray Drying facility is available for spray drying process development and contract manufacturing.



GEA Process Engineering

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