Commercialising discovery with Niro spray drying

Niro Technologies

GEA Pharma Systems

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.

Go from drug discovery to drugstore faster with spray drying

Perhaps ironically, developing medicines has always been a rather painful business. Unearthing new compounds, isolating APIs, formulating therapies, conducting clinical trials, gaining approval, securing patents, winning doctors' confidence - it all takes a lot of time, money and energy. Of course the rewards, financial and personal, make it well worthwhile.

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

Yet despite all efforts, the chances of ending up with a blockbuster in your hands remain incredibly slim - and declining. R&D productivity is under real pressure while investment is at record highs. The challenge in recent years has not only been finding new compounds, but formulating known discoveries into commercial products.

Many potential treatments sit stranded between basic research and prescription medicine due to issues such as insolubility, instability and delivery system. What's more, this trend is gathering momentum as companies explore new routes to drug discovery, such as biotechnology research.

Spray drying is a breakthrough technology that offers R&D staff a unique remedy to some of the formulation challenges facing the modern pharmaceutical business.

Specifically the unprecedented particle control achievable with spray drying opens the way to employing previously unattainable delivery methods and molecular characteristics.

These advantages not only remove many of the obstacles to turning new discoveries into commercial drugs, but can also provide new avenues for life-cycle management and patent extension.

Widely used in the chemical and food industries, spray drying has been adapted to meet the exacting standards of the healthcare sector by Niro. The world's leading supplier of pharmaceutical spray dryers, Niro has spent more than a decade refining its technology specifically for use within the area of final solid dosage drug forms.

Five ways spray drying can help you commercialise discoveries

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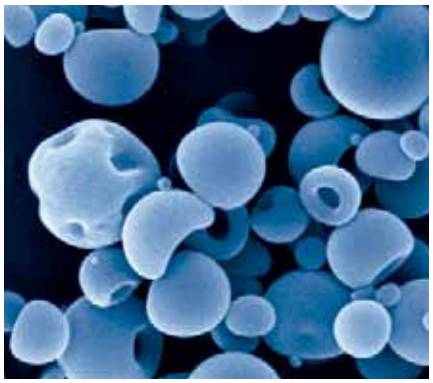

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1. Bioavailability

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

With spray drying you can 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 speed that allows the API to be captured in an amorphous form.

By enhancing the dissolution rate in this way, spray drying has the potential to open the door for new, important treatments that are currently shelved due to low bioavailability.

2. Modified release

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 illnesses, e.g., cancer or AIDS, and reduce side effects. On a more practical level, the technique is employed for taste masking and the physical protection of the API.

Spray drying as well as spray congealing makes it possible to create particles in order to fashion specific release patterns and other properties. For encapsulation, the API and biodegradable excipients are dissolved and/or suspended, or melted together in case of spray congealing. Subsequently the mixture is atomized and dried into a powder.

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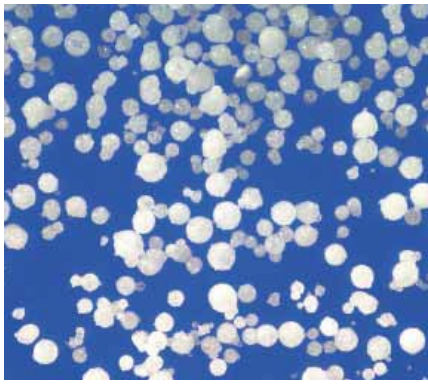

- Bioavailability
- Modified release
- Aseptic Production
- Inhalation
- Compressibility

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

Producing stabilised vaccines using spray drying reduces the need for refrigeration and makes their transport and storage far easier. Currently a staggering 50% of all vaccines in the developing world - where they are most needed - are damaged due to lapses in the "cold chain".

4. 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, 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.

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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.

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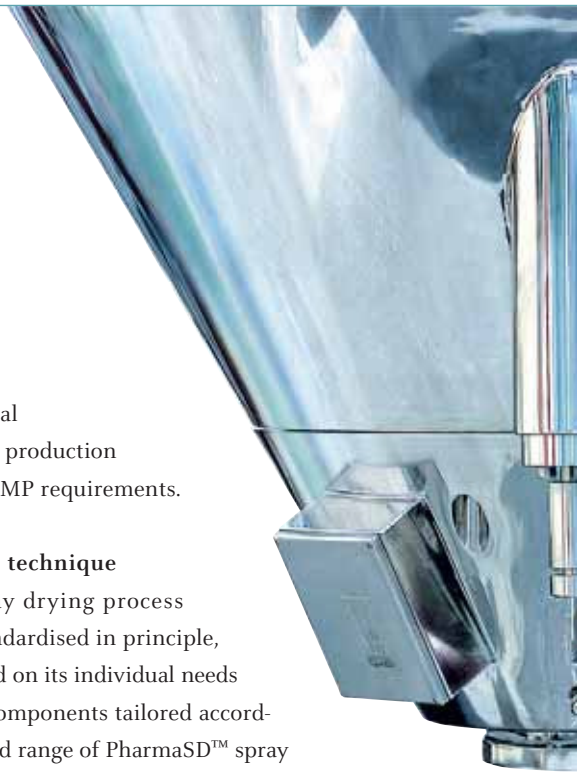
5. Compressibility
Solid dosage pharmaceuticals have often required a separate granulation step in the production cycle to avoid segregation and to produce a powder that has the correct flow properties to accommodate a high-speed tablet press.

However, in the case of spray drying, granulation can be made an integral part of the continuous process, a technique pioneered by Niro. This not only results in a more streamlined, efficient production process, but reduces costs too.

Just what the doctor ordered

Niro's aim is nothing short of giving the R&D capabilities of pharmaceutical companies a shot in the arm. By giving drug formulation efforts fresh options when it comes to particle form and delivery method, it is our firm belief that spray drying can play a role in bringing a new generation of solid dosage drugs to market.



It's a belief anchored in experience. For 75 years Niro has been the world's leading supplier of spray drying technology. Over the past decade Niro has extended its range to include dryers for drug delivery applications. As a result we have substantial experience of working in partnership with the pharmaceutical industry.

This alliance is clearly reflected in every detail of our dedicated pharmaceutical spray dryers range. Our equipment and processes take into account the unique character of today's pharmaceutical business. And in terms of scale, dryers range from laboratory size for R&D work, to industrial plants for commercial production in accordance with cGMP requirements.

A verifiable, precise technique

While the basic spray drying process and technology is standardised in principle, each project is assessed on its individual needs and the process and components tailored accordingly. Niro's unmatched range of PharmaSD™ spray dryers is built on a modular design, allowing components to be integrated depending on the requirements of individual projects.

As a well-established continuous process offering excellent control capabilities, spray drying can be used in conjunction with process analytical technology (PAT). In this way critical process parameters can be continuously monitored and documented.

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

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

The atomizing device, process gas disperser, drying chamber, cyclone and bag filter are always chosen according to the feed characteristics and the final product requirements.

Five things you might not know about spray drying

1. Spray drying is suitable for heat sensitive materials

Spray drying is already used for the processing of heat sensitive materials (eg, proteins, peptides and polymers with low Tg 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

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 met, 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

Niro has ample 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:

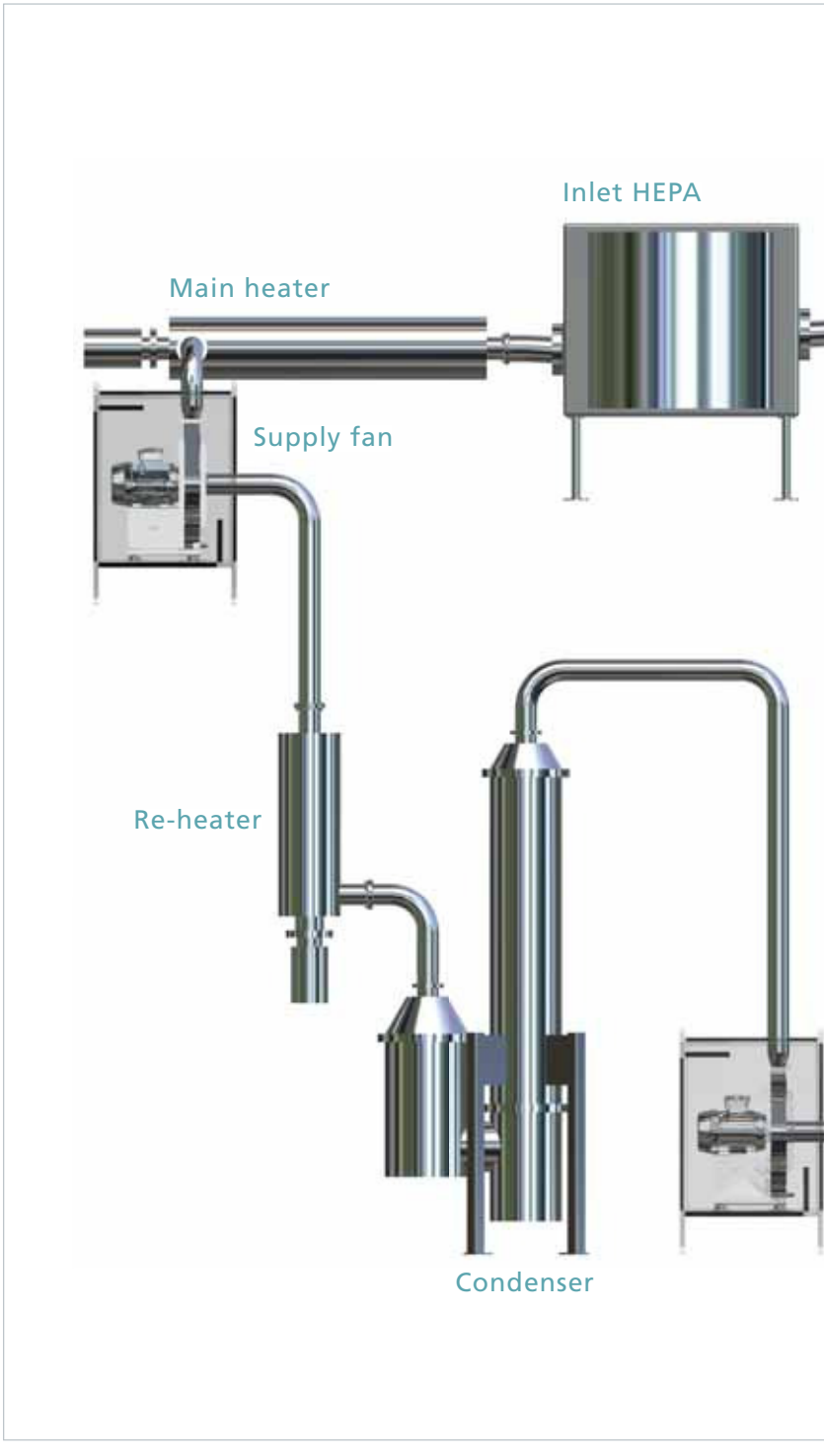
a. **Atomization**: A liquid feed stock is atomized into droplets by means of a nozzle or rotary atomiser. Nozzles use pressure or compressed gas to atomize the feed while rotary atomizers employ an atomizer wheel rotating at high speed.

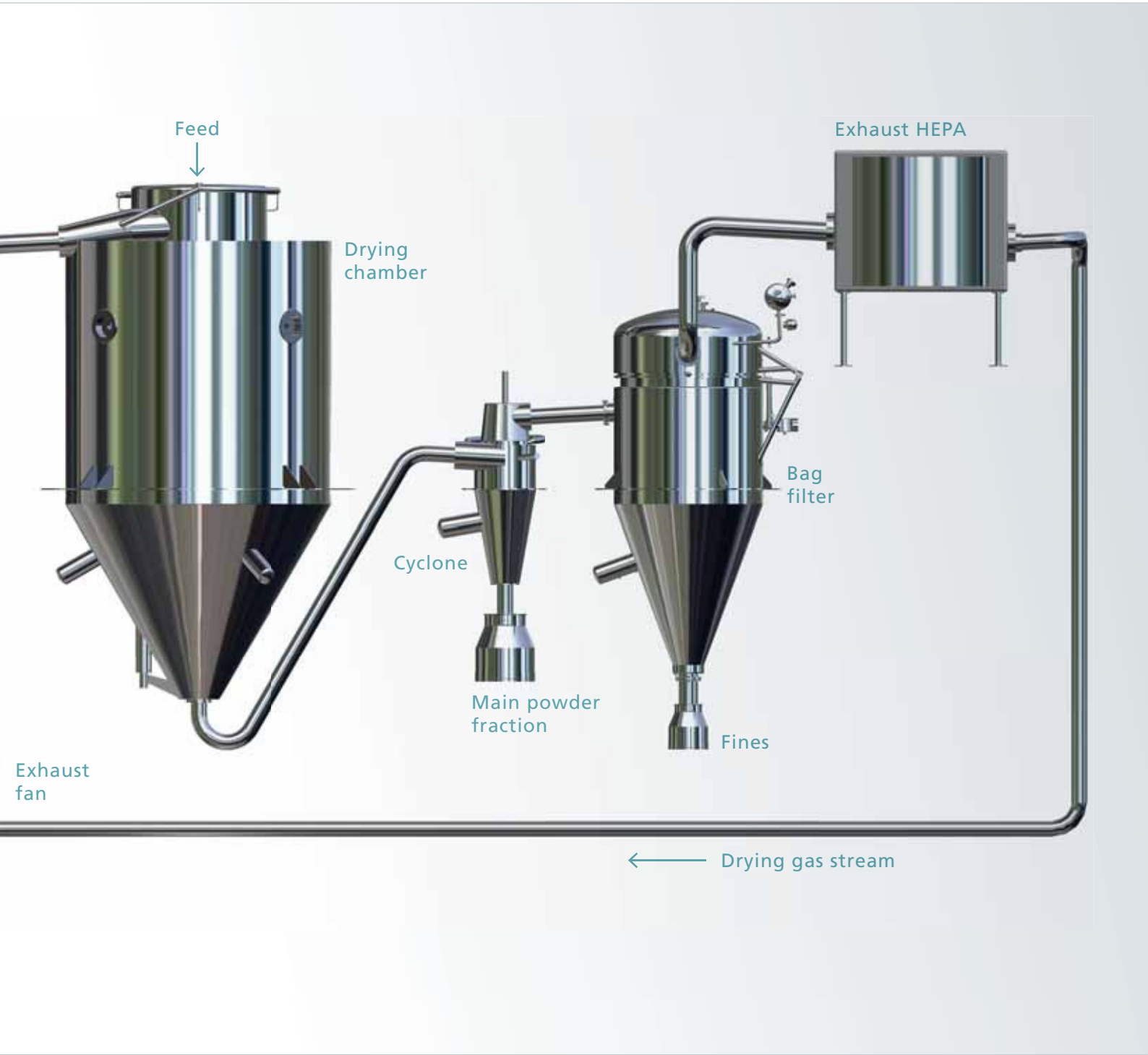
b. **Drying**: Hot process gas (air or nitrogen) is brought into contact with the atomized feed using a gas disperser, and evaporation begins. The balance between temperature, flow rate and droplet size controls the drying process.

c. **Particle formation**: As the liquid rapidly evaporates from the droplet, a solid particle forms and falls to the bottom of the chamber.

d. **Recovery**: The powder is recovered from the exhaust gases using a cyclone or a bag filter. The whole process generally takes no more than a few seconds.

Closed cycle spray drying system




Feed
Exhaust HEPA
Drying chamber
Bag filter
Cyclone
Main powder fraction
Fines
Exhaust fan
Drying gas stream

A surer path to a healthy business

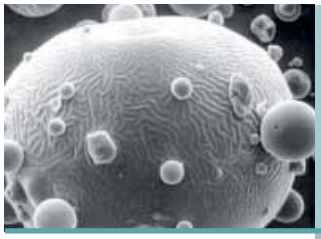
At Niro we know there's a lot more to formulating therapies than having the right equipment. That's why we've never considered ourselves an equipment supplier but rather a process development partner. We can help with all aspects of investigating how spray drying could enhance your drug formulation.

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 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 tech-transfer time.

Beyond steel

Apart from hardware, collaborating with 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

Niro's international Pharma Test Station is the only GMP facility of its kind, 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 our customers in drug development projects.

The concept behind our facility is to allow customers 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 customers to train staff and qualify processes in parallel with the commissioning of a commercial production unit. This substantially compresses the time used in the switch to commercial production during the final phase of the development cycle.

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.

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.

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.

www.geapharmasystems.com

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.

GEA Pharma Systems

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