FREUND

PHARMACEUTICAL SPRAY DRYING

Creating New Business Opportunities and Revenue Growth for Drug Makers

www.freundglobal.com | sales@freundglobal.com

Introduction

Spray drying technology has been around for more than 150 years. First used in 1872 for “powderizing” milk, spray drying continues to be widely used for production of powdered instantized milk. But it’s only been during the last 30 years that its seen rapidly increasing use in the pharmaceutical industry, especially for improving the solubility profile of poorly water-soluble Active Pharmaceutical Ingredient (API).

Following are several cases where drug makers might benefit from spray drying technology. These points may help readers examine their own business strategies and drug portfolios, combined with their business planning, to see if spray drying can help them generate new revenue streams. Several opportunities are explored in this paper:

1. Solubility enhancement for poorly water-soluble API.
2. Encapsulation technique for taste masking and for engineered drug release profiles.
3. Processing substances that are subject to thermal degradation.
4. Production of drug products for dry powder inhalation (DPI).
5. Product line extensions and new product innovations from 505(b)(2) regulatory filings.

"The introduction of spray drying technology into a pharmaceutical manufacturing business can provide new opportunities for product line expansion, business growth, and channels to increase revenue and profits. This can be from creation of new products that cannot be produced any other way. But it can also allow for line extensions of existing products and alternate drug product solutions for known API’s already offered in the market today."

Greg Smith
Vice President, Global Sales

(1) SOLUBILITY ENHANCEMENT WITH AMORPHOUS SOLID DISPERSIONS

Many drug substances have been proven to have good efficacy to treat illnesses. But commercial interest in these substances has been limited by poor solubility and the resultant high drug loading required for patients to receive therapeutic dose. This is largely apparent with Active Pharmaceutical Ingredient (API's) falling into the Biopharmaceutics Classification System (BCS) II and BCS-IV categories for permeability and solubility.

In simple terms, spray drying for solubility enhancement involves creation of a stable, molecular dispersion of API in a solid polymer matrix. The process involves dissolving crystalline API in organic solvent along with a suitable polymer. This solution enters the process by by feeding with a pump to the spray nozzle, where it is atomized. The resulting droplets mix with the heated stream of drying gas (commonly pure nitrogen) where they are dried to create powder with predictable and well-defined particle characteristics. The API is far more soluble in a molecular presentation to the patient than it is in crystalline form.

This emphasis on solubility enhancement is important because of the potential value proposition to drug manufacturers. Drug products can be produced in ways that are not possible with any other process or equipment. This area of the pharmaceutical industry is expected to grow at a rate of about 10-15% CAGR, which is twice the growth rate across the pharma industry in aggregate.

Industry experts report that as many as 70% of all New Chemical Entity (NCE's) exhibit either poor solubility, poor permeability, or both. In addition, many drugs already on the market suffer from these same limitations, which results in unnecessarily high drug loadings to compensate for low rates of adsorption. Using spray drying as an enabling technology, it may be possible to deploy APIs into the market with commercial viability not previously possible.

(2) ENCAPSULATION TECHNIQUE FOR TASTE MASKING AND FOR ENGINEERED DRUG RELEASE PROFILES

Encapsulation techniques are already widely used for taste-masking, gastric protection of drug substances, creation of modified release profiles and for extended release over time. Technologies already in use for encapsulation are fluid bed processing, high shear granulation and bead coating for multi-particulates and micro-tabs. For a drug company already using these techniques, spray drying can offer another technique to their capabilities.

In some cases, drug product line extensions can become profitable by creating new formulations that can be processed in a spray dryer. And because spray drying is a continuous process, additional savings may be possible by reducing the amount labor, material handling and record keeping that is ordinarily used for batch processes. That is, one spray drying campaign can take the place of multiple batches run in a fluid bed. It may be useful for manufacturers to consider this approach on new drugs in their pipelines.

(3) PROCESSING SUBSTANCES THAT ARE SUBJECT TO THERMAL DEGRADATION

For substances that are susceptible to damage from continuous exposure to elevated temperatures, which is common in batch processes, spray drying can be an attractive processing method to consider. In a spray dryer, the atomized solution droplets are exposed to drying gas for only a very short period (just a few seconds). Heat is given up during rapid evaporation to provide a cooling effect for the dry material before it exits the drying chamber.

This principle of the spray drying process helps it compete well against some other technologies that are used to produce solid dispersions. Hot Melt Extrusion (HME), for example, is one of these techniques. HME uses heat to melt the polymer and this also exposes the API to high temperatures which may cause degradation that adversely affects a drug product's stability and efficacy. Because spray drying spares APIs and sensitive excipients from damage and thermal degradation, the drug maker can benefit from lower material supply costs, higher manufacturing efficiency, reduction in waste and a high standard of product quality with predictable shelf life.

Drying Chamber Extension
Adding one or more drying chamber extensions increases chamber volume to promote longer exposure, especially for slow drying of small dense particles and while processing heat sensitive substances at low temperatures.

(4) PRODUCTION OF DRUG PRODUCTS FOR DRY POWDER INHALATION (DPI)

While solubility enhancement is important for certain drugs, it may still not be adequate for a suitable product to succeed as an oral dosage form. For this reason, manufacturers might create spray dried powders for pulmonary delivery achieve desired efficacy and also to permit more favorable receptor targeting. Inhalation bypasses the oral route and eliminates the variables of gastric chemistry and adsorption in the intestinal track.

Dry powders for inhalation must be produced within a narrow aerodynamic particle size range of just 1-5 micron. Particles that are too large cannot pass into the fine blood vessels in lung tissue. Particles that are too small may not be absorbed and can be lost when the patient exhales.

Due to material limitations, recovery efficiency, and the challenges of handling fine cohesive powders, this technique has been embraced in a limited number of cases on large production scale systems. Still, there are companies today working on innovations to allow pulmonary delivery of challenging small-molecule drugs and for biologics. For high value products, an investment in spray drying technology may provide substantial return on investment.

(5) PRODUCT LINE EXTENSIONS & NEW PRODUCT INNOVATIONS USING AN FDA 505(B)(2) REGULATORY FILING PATHWAY

Spray drying is an enabling technology that can help a drug maker extend the life of their proprietary products. It allows for use of Active Pharmaceutical Ingredient (API's) that are already thoroughly understood and even in use for existing approved drugs. All the in vitro experiments, toxicology, efficacy, and clinical studies are already complete, which greatly reduces the financial barrier to bringing new drugs to market. With regulatory barriers diminished because of all the prior work, drug products might be brought to market rapidly and with lower upfront costs when following a 505(b)(2) filing pathway.

In Europe, Article 10 of Directive 2001/83/EC provides a "hybrid pathway" that's similar to USFDA 505(b)(2).

Following are two examples where a 505(b)(2) filing pathways may be beneficial to the drug maker and for the patient:

- Changing the dosage form route of administration, such as a change from oral delivery to inhalation.
- Change to drug loading: The chemical API is the same substance, but API content of tablet or capsule may be reduced through solubility enhancement. This lowers the API content in each dose. This may result in lower cost to the drug maker for API procurement, lowered risk of patient overdosing and improved consistency of the drug uptake in the patient.

Other benefits of 505 (b)(2) filings:

- Exclusivity and Protection of Intellectual Property:
  - If spray drying can be used to enhance solubility of challenging substances for treatment of cancer, CNS disorders and rare diseases of all kinds, it may be possible for the drug company to enter the orphan drug market. This can have huge financial rewards by taking advantage of reduced costs to develop and commercialize therapies using a 505(b)(2) filing.
  - This avenue may also provide market exclusivity per USFDA in 21 CFR 314.20-316.36. (There may be similar pathways in other countries).

- Spray dried formulation for 505(b)(2) drug filings may also open new revenue channels if the company wants to enter the growing market for advanced pediatric formulations and child-specific dosing. This is covered in section 505A of the USFDA Act.

Longstanding Trusted Source, Constant Innovation

The technological know-how developed by FREUND has resulted in a diverse range of products and services.

FREUND

sales@freundglobal.com
www.freundglobal.com

Rev 4/2026