

Reducing the risk of drug development and production for Synthon BV

GEA Pharma Systems (GPS), part of the GEA Group, has helped develop a complete process line for one of Europe's most successful pharmaceutical companies for the manufacture of generic medicines.

The 'Pellet Processing' project includes the supply and integration of; granulation technology with a Collette™ UltimaGral™ and Aeromatic-Fielder™ [NICA™ Pelletizing System](#), Coating technology with GPS's unique PRECISION COATER™ and Fluid Bed Drying.

[Synthon BV](#)

Based at Nijmegen in the Netherlands, Synthon manufactures a range of products for worldwide distribution through its marketing partners in Europe, the USA, Canada, Australia, New Zealand, Chile, Argentina and South Africa. The development of the generic version of a drug will usually begin several years before the expiration of the patent with the aim of introducing it to the market within a few hours of the protected period ending. Synthon focuses on the more complex pharmaceuticals as fewer of its competitors have the human and technical resources to replicate them.



Development of the generic version of a drug

Initially small batches of the drug are produced in the laboratory before up-scaling production to meet the demands of the market. Up-scaling production from a laboratory batch size of 200g to a typical production batch size of 500kg while maintaining the exacting standards of the formulation represents a major challenge to drug manufacturers. The choice of equipment and the expertise available from its manufacturers plays a key role in getting the product to market quickly and maintaining the required standards in production.

Investment in GPS equipment to coat tiny pellets

After evaluating the systems offered by the GPS group, Synthon approached the company in 2002 when new equipment was required for a partner manufacturing plant in Greece to up-scale production of one of its products. The first requirement was for the NICA™ extrusion/spheronization equipment to manufacture tiny pellets containing the active ingredient followed by the PRECISION COATER™ with its unique airflow characteristics, giving a very exact and even coating of product both technologies supplied by Aeromatic-Fielder. Coating of the tiny pellets, which can be less than 1 mm diameter, is necessary for several reasons, for example to mask unpleasant tastes, improve appearance or, as in this case, to provide controlled release of the drug in the body. The aim is to evenly coat the pellets with just enough material to achieve the desired result and no more.

Why Synthon chose the Nica™ System

Additional NICA™ pelletizing equipment was subsequently supplied and integrated with the system to manufacture the pellets themselves. Synthon chose the NICA™ equipment, partly because of its exceptional performance and flexibility, but the co-operation of GPS as a business partner played an important role. “We looked carefully at what equipment was available commercially to do the development work,” said Synthon’s director of technology Derk Sanders. “After looking at all the possibilities we decided on the GPS Nica™ system for our development and up-scaling activities. GPS allowed us to rent the necessary equipment to produce batches under GMP requirements. The whole exercise went very well and we subsequently upgraded the systems to the largest available from GPS. We now have three NICA™ integrated extruders/Spheronizers producing a total of 2700kg a day”

Derk Sanders cited the simplicity of the GPS equipment as being a key factor in the successful development of the process. “Production has now been underway for just over a year with around 300 batches of the drug produced,” he said. “So far not a single batch has been rejected due to failure of the equipment.”

One of the main obstacles for pharmaceutical companies in the development of drugs is the cost of trials. The use of the test centre in Bubendorf significantly reduces these risks giving manufacturers confidence that critical manufacturing processes are viable without major capital expenditure.

GPS test centre facilities ... an “important resource”

The GPS technology centre in Bubendorf Switzerland, which opened in 2003, has been used extensively by Synthon to develop its production processes. The technology centre provides pharmaceutical companies with a one-stop GMP environment to enable them to develop new solid dose products using the latest equipment. The centre is equipped with the full range of GPS equipment from powder mixing, through granulation and drying to tablet pressing and coating.

“The technology centre is a very important resource for Synthon. One of the main benefits is that it enables us to test our processes using small quantities of API (Active Pharmaceutical Ingredient),” continued Derk Sanders. “We need to know that the equipment we select for production will produce the formulation in large batch sizes and the facilities at the centre allow us to do that. To do the same test here in the factory would require API test batches of 500kg which would be a huge risk and prohibitively expensive. Our R&D department is using the centre more and more to help develop processes for future products.”

“We have a very good relationship with the technology centre and they’ve been very flexible in accommodating us, often at short notice. We’re a dynamic company and we have to move quickly to stay ahead, they have always given us excellent service: it is a partnership.”

GPS added, “Having the technology centre means that we can work closely with customers to conduct tests and make sure the equipment is suitable for an application before they place an order. This safeguards the customer’s interests and allows us to prove the system we are recommending. It’s a perfect tool for us.”

The vast practical experience of the machine operators is a further advantage of using the test centre. During testing, conditions are often taken to levels far beyond those experienced in normal production. The data collected often shows that conventional

processing techniques can be modified with beneficial results.

Sharing valuable information for use in future projects

Development engineers from Aeromatic-Fielder's factory in the UK make frequent visits to the test centre to see at first hand the machines working in a production environment. This provides Synthon's R&D engineers with the opportunity to share information and give feedback to the equipment manufacturers. This regular close contact provides Synthon with valuable information for use in future projects.

A strong future for GEA Pharma Systems and Synthon

GPS's relationship with Synthon has grown during the last 4 years and looks set to become even stronger in the future. "Our experience of working with GPS has been very favourable," said Derk Sanders. "Business is always a two-way thing and both companies have worked together to achieve excellent results. I am very comfortable with GPS and I look forward to working with them in the future."

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