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CASE STUDY

MUPS specialist Acino trusts in Romaco Innojet



KAI KOCH,
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Kai Koch, Engineering Manager, Romaco Innojet, in this case study highlights how Romaco Innojet machines, with its air flow bed technology, have enhanced production at Acino Pharma's Liesberg facility

ACINO, THE Swiss pharmaceutical producer, has trusted in Romaco Innojet technologies to make its MUPS tablets ever since 2004. Five processing machines in the VENTILUS series are currently used to coat micropellets at Acino's Liesberg facility. There is a steadily growing demand worldwide for innovative oral release forms.

The backdrop is breathtaking, about 20 miles south of Basel, surrounded by the mountains of the Swiss Jura, is the site of Acino Pharma's Liesberg production facility. The Acino Group, headquartered in Aesch, is specialised in the development and production of complex galenic formulations. The manufacture of pharmaceutical solids with delayed API release is one of the Liesberg plant's core competencies. Around 1.5 billion tablets and capsules currently leave the factory every year.

"In spite of this, our capacities here are not yet exhausted and our international target markets are growing at exponential rates. That's why we're planning to double our volumes in the medium term," explains Christophe Dohr, Pharmaceutical Production Head Liesberg, Acino Pharma.

Acino Pharma presently employs some 110 staff in Liesberg, with production in



Acino production VENTILUS



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The Acino Group, headquartered in Aesch, is specialised in the development and production of complex galenic formulations

three shifts, five days a week. The majority of the output is destined for licensees both in Switzerland and worldwide. Acino's portfolio at the Liesberg



Romaco Innojet Rotojet

site comprises oral drugs for treating cardiovascular disorders and Parkinson's disease as well as various narcotic substances. So-called MUPS tablets form the mainstay of its business.

MUPS and their many advantages

Multiple unit pellet systems, or MUPS for short, are a dosage form consisting of coated API pellets, which are mixed with microcrystalline cellulose and pressed into tablets. Their main characteristic is the controlled release of the active ingredient, which is achieved by applying a functional coating to the pellets. The medication is absorbed in the intestine once the tablets have dissolved in the stomach. Since the tiny pellets pass through the digestive cavity rapidly and unhindered, MUPS tablets do not necessarily have to be taken on an empty stomach. They can also be halved without losing their therapeutic efficacy. Cutting the tablets in two does not damage

the sustained-release coating of the micropellets. All of these criteria help improve patient compliance.

The demand for MUPS formulations has risen steadily in the last few years for these diverse reasons. In particular, tablets are a dosage form to which most patients are already accustomed. Acino was among the first to recognise this trend and position itself accordingly. Today, more than 90 per cent of all pellet batches are pressed into MUPS tablets. "Acino specialised in the manufacture of MUPS tablets over a decade ago. The highly complex production process has been continuously improved ever since and we're now in a comfortable situation where we can deliver premium quality at attractive unit costs," Dohr emphasises.

Two-stage coating process

Before being pressed into tablets, the pellets undergo a two-stage coating process in which their weight is more than doubled. Neutral pellets made from glucose are used as starter particles. In the first step, the active pharma ingredients are applied one layer at a time, followed by the sustained-release coating. This process takes several days, during which the diameter of the pellets increases from approximately 300 µm to 1000 µm (micrometres). The micro format gives a good idea of the complexity involved.

Since 2004, Acino has trusted in the air flow bed technology originally developed and internationally patented by Dr h.c. Herbert Hüttlin to build up these pellets. Five Romaco Innojet production machines in the VENTILUS series are installed at Acino's Liesberg facility together with a pilot system of the same type, which is used for research and development. The containers of the production scale machines have a capacity of 800 litres and are designed to handle batches weighing up to about 600 kg. Despite its sheer physical size the technology saves valuable space on the production floor. "The air flow bed unites all the processes which are necessary to build up API pellets and granulates in

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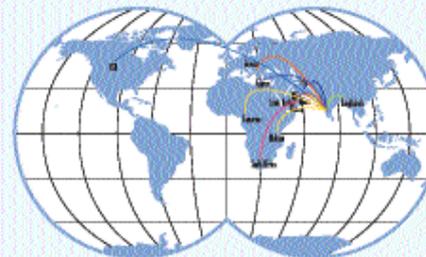
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Acino Liesberg site

one system,” confirms Michael Tewelde, Team Expert Granulation, Acino Pharma. “Alternative technologies would need a much bigger footprint, not to mention the additional storage capacity.”

Air flow bed technology

The process air used for the air flow bed is controlled by the special booster – an ingenious container bottom consisting of overlapping circular plates. The homogeneous flow conditions which are created in this way result in a spiral, orbital product flow. The process air causes the pellets to hover, so that gentle intermixing is guaranteed and particle collisions or friction are avoided. The speed of the pellets and the distance travelled are clearly defined. The evaporation rate can therefore be calculated precisely and the dose rate adapted to match. The coating material is sprayed into the product from below by a central bottom spray nozzle. This nozzle is designed with a rotating spray head which prevents the annular spraying gap from



Acino MUPS sample

becoming blocked. The gap has an adjustable width, enabling the droplet size to be varied. In addition, the spray angle can be set exactly by means of the spraying and support air and there is virtually no measurable spray loss. The pellets pass through the liquid film regularly. Be-

fore the next coating is applied, they must be sufficiently dry for the product not to be over-wetted. The spray rate can be adjusted to rule out unwanted agglomeration due to the carrier dissolving. “The Ventilus technology lets us regulate moisture extraction absolutely accurately;

that way, the pellets are built up homogeneously with only a very small standard deviation,” Tewelde continues. “They’re spot on in terms of quality and process efficiency.” Owing to the selective application of the suspension, Acino’s consumption of raw materials and coating is more-

Acino has an in-house test laboratory in Liesberg with air flow bed systems for laboratory and pilot trials. Many customers take advantage of this opportunity to test their formulations during the development phase

over down between ten and fifteen percent, saving further time and money.

Acino’s Liesberg lab

Acino has an in-house test laboratory in Liesberg with air flow bed systems for laboratory and pilot trials. Many customers take advantage of this opportunity to test their formulations during the development phase. Scale-ups from pilot to production are a regular event there on a VENTILUS V 200. Video cameras which show the product movement directly on a screen are installed in all Innojet systems to permit the coating processes to be monitored. The operator can thus keep a close watch on the batch process at all times and intervene immediately if necessary. And for interested customers, it’s a unique chance to see the MUPS coating technology live in action.