



The equipment, here a film coater of the GC2 series from Glatt, is subjected to over-pressure and dust-proof sealed off.

Sources: R-Pharm

BALANCING ACT OF GRAMS AND KILOGRAMS

An innovative room containment concept provides contract manufacturer R-Pharm Germany unmatched flexibility in small batch production — after prize-winning Newcon, R-Pharm lands a new coup with the Product and Process Development Center (PPDC). The new development center is a highlight in flexibility and high containment.

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Idylic is the word that comes to mind when most people think of the quaint town of Iltertissen on the river Iller. But insiders know the small Swabian city has much more to offer than just a great landscape and a historic city center: it also houses plenty of high tech potential. To

be more specific, the town is home to one of the most innovative high-containment factories of recent years. Contract manufacturer R-Pharm was named “Facility of the Year” by Ispe in 2008 for its Newcon, or New Containment. Glatt from Binzen has been a technology partner of R-Pharm since



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ANDREAS HÄNEL
R - PHARM

the 1990s, delivering production-scale tablet coaters and other equipment to the containment factory. Ever since, Illertissen has been more than an insider tip for anyone interested in fully-automated containment production.

Quality and Employee Protection

The system makes it possible to process highly active substances with exposure limits well below 0.1 micrograms per cubic meter (OEB class 5) in a fully-automated environment without manual intervention during normal operations. No other company today offers a higher degree of process automation in the pharmaceutical industry, and using the newest technologies for in-process analysis not only makes production highly efficient, but also ensures high product quality and provides the best possible occupational protection to operating personnel.

New development center closes the gap

R-Pharm has even more to offer as of last year. The contract manufacturer opened its Product and Process Development Center—or PPDC for short—closing a gap between product development and commercial production in the field of highly-active pharmaceuticals. In addition to cost-efficient containment solutions for fully-automated production processes, the market today is demanding ever smaller minimum quantities of highly potent solids, with the best possible flexibility. “Because of this, we need to be able to handle all development and production steps in producing sol-

id forms,” explains Andreas Hänel, manufacturing manager at R-Pharm. That’s why the PPDC offers tablet and granule development, all the way to full formula development. We are able to produce batch sizes from 0.5 to 20 kg in the production area. We offer grinding, mixing, and filtering processes, dry and moist granulation, capsule filling, tablet production, and coating and pelletization. Technology partner Glatt was also involved in planning and implementing the PPDC. The PPDC is the pharmaceutical company’s way of putting the icing on the cake of its past activities, so to speak. The management has developed the location into a center of competence for “high containment manufacturing” over the last 15 years. There are four different containment facilities in Illertissen with different degrees of automation for batch sizes between 0.5 kg and 700 kg. Ultimately, contract manufacturers can’t just pay lip service to flexibility. Instead, it’s a necessity and a key competitive factor. Downtimes cost money, and only a system operated at high efficiency can process customer orders quickly and optimally. In order to achieve good flexibility and load, the new production suite develops, produces and packages both conventional (OEB 1-3) and highly active solids (OEB 4-5). This is kind of like squaring the circle, as the company works to juggle different production requirements. But 15 years of containment expertise are definitely a valuable asset to the pharmaceuticals manufacturer. “We gained a lot of experience while building the Newcon that helped us construct the development center,” Hänel emphasizes.

PROCESS-Tip

A video about the Newcon and the PPDC can be found with further extensive information about R-Pharm at www.process.de.

For example, it became clear very quickly that a classic isolator concept would restrict the flexibility we needed. Development and small-batch production take a lot of manual labor: Equipment can change frequently, devices need to be cleaned often, samples are taken, etc., which is why R-Pharm used a room containment concept. Specifically, this means that processing is completed in a climate-controlled room at negative pressure that is hermetically regulated via a sealing system to ensure outside areas are not contaminated. Pharmaceutical technicians work in ventilated protective coveralls when handling OEB 4/5 drugs. All of the equipment is mobile and equipped with castors that allow it to be moved as needed. This lets em-

ployees combine equipment for each specific task, then decontaminate it after it's used in the cleaning room. That means qualifications, maintenance, and cleaning of unused machines can be completed at the same time as ongoing processes. "This gives us the mobility we simply need for development," Hänel explains. Although this sounds relatively simple, in reality it was a major challenge for equipment manufacturers, as the equipment needed to be exposed to excess pressure and sealed to ensure no dust would penetrate it. "We simply couldn't use off-the-shelf systems," Hänel emphasizes. The biggest problem is heat development, since stand-alone devices

all have switch cabinets with ventilation slots—a major problem when it comes to dust. If you need to seal off those slots, where does all the heat go? Especially for fluidized bed systems, Glatt technicians needed to play the

trickster to get equipment ready for containment. "An ingenious ventilation system was used to vent heat from the machines out of the technology area, while at the same time preventing dust penetration—a highly

effective solution for both problems in 'one fell swoop,'" explains Michael Maintok, containment expert at Glatt. Glatt provided seven small batch coaters and granulators with appropriate technical adaptations to the PPDC for granulating and coating.

Smart room concept prevents cross-contamination

The entire production area consists of three rooms: two production rooms and a cleaning room between them. That means the "hot zones" for core processes are spatially separated and have different climate control systems, while other areas can be used together. After a campaign, the employees can push used equipment through the lock and into the adjacent cleaning room, then from there into the neighboring production room, where it waits clean and ready for its next use. The safety laboratory used to analyze highly active substances is also new.

The PPDC is connected to the "high potent lab" via alpha/beta ports. Isolators, safety work benches, and flues ensure safe working conditions without additional protective equipment. This equipment will also be useful in the future, if even more potent materials are used for development.



In demand at R-Pharm Germany Managing Director Dr. Holger Weyhers

SUCCESS FACTOR CONTAINMENT

What were the most important reasons to invest in the high-containment development center?

DR. HOLGER WEYHERS: By commissioning the "PPDC" (Product and Process Development Center) multi-use system, we are supplementing our contract manufacturer services and becoming a "full service CDMO" for solid pharmaceuticals. This lets us close the gap between product development and commercial production in the highly active pharmaceuticals sector. Our customers can benefit from the wide variety of custom-tailored containment solutions we've implemented over the past 15 years.

What special features does the development center have?

WEYHERS: Our development center is based on a finely tuned spatial concept with mobile equipment in a containment environment. This allows us to achieve a high level of efficiency in using and cleaning our equipment. We couldn't use an "off-the-shelf" solution, since we use a room containment solution that allows for direct intervention in the process. We needed to adapt available system configurations to our flexible concept.

What motivated you to work with Glatt once again?

WEYHERS: We have been working with Glatt equipment since the mid-1990s. We decided to trust in our long-term design and process technology partnership with Glatt for the new project as well. We also value the high quality of their equipment. Using Glatt systems in the development center also made it easier to scale up our existing systems.



Conceptual design of Product and Process Development Center