

INDUSTRY application

Shanghai Roche retrofits tablet press for high containment

Shanghai Roche Pharmaceutical was established in 1994 as a venture between Sunve Pharmaceuticals, Shanghai, China, and F. Hoffman-La Roche Ltd., Basel, Switzerland, a research-intensive health care company that specializes in pharmaceuticals and diagnostics. The company produces antibiotic, anti-cancer, transplantation-immunity, and cardiovascular products, mainly for consumers in China, Hong Kong, and South Korea. At first, Shanghai Roche had only a non-high-containment solid dosage manufacturing line, but in 2005, the company added a high-containment facility to manufacture high-potency products. In addition to its conventional and high-potency solid manufacturing lines, the company operates two sterile product manufacturing lines, which produce antibiotics and water for injections, and several packaging lines.

To protect tablet press operators and other workers, Roche's global standard requires that the anti-cancer and transplantation-immunity drugs be produced without exposing operators to APIs in concentrations that exceed 0.01 milligram per cubic meter (mg/m^3). (That amount is product specific, not valid generally.) This is



Shanghai Roche installed an isolator to reduce API concentrations to $0.01 \text{ mg}/\text{m}^3$, protecting the operators.



The isolator doesn't interfere with powder flow, tablet compression, or tablet movement.

known as the internal occupational exposure level (IOEL). "Before we established the high-potency plant,

the operators manufactured products using personal protection equipment (PPE)," said David Fang, who is the

production manager responsible for conventional and high-potency solid dosage manufacturing. "The purpose of the high-potency plant is to establish a containment production line so that the entire IOEL can be lower than the standard and the operator can run the system without PPE."

Fang said that Shanghai Roche sought the help of its equipment vendors to provide containment, and it was a successful approach in some areas of the high-potency facility. But Fang still saw room for improvement in dust containment in the tableting operation.

Buy new or retrofit?

Fang and his colleagues weighed the advantages and drawbacks of installing a containment-ready tablet press with those of retrofitting the existing machine. Clearly, new equipment would solve the problem, but Fang said that the containment-ready tablet presses they considered were very expensive and would have required considerable time for installation, commissioning, and validation.

Instead, Shanghai Roche opted for a retrofit isolator called TabCell from Powder Systems Ltd. (PSL), Boise, ID. "I was attracted by the compact isolator, the compact air handling system, and the design of the charge port from PSL," Fang said. "I wasn't familiar with the company, but our project manager was, and another Roche plant was already using the equipment."

The company can manufacture highly potent products without personal protection equipment.

The TabCell is a glove box isolator that retrofits around an existing tablet press to contain airborne powder that could otherwise escape during operation. It allows access to the tablet press via a flexible gloveport window. Safety interlocks between the press's gloveports and moving parts prohibit access when the equipment is in operation. The straightfor-

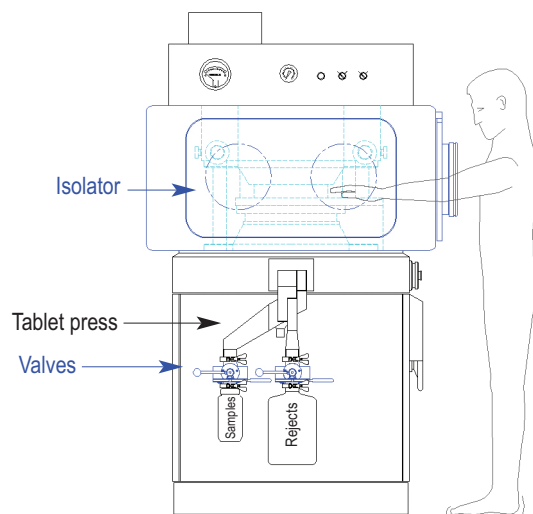
ward construction allows the supplier to build and ship the isolator on short notice and retrofit it onsite with minimal downtime.

In late 2005, Shanghai Roche finalized the project details, and by the summer of 2006 the retrofit was installed and the tablet press was ready for testing. "The PSL engineers helped our engineers install the isolator," Fang said. "They spent 7 to 10 days on site for the installation, site acceptance tests, and training. It was very simple."

The isolator is installed around a Manesty Unipress tablet press and creates and maintains a carefully balanced negative-pressure environment to contain dust without affecting powder flow, tablet compression, or tablet movement. It also uses HEPA filtration. At the same time, it allows easy access for operation and maintenance without compromising safety. "The safety interlocks and the internal barriers are very important to Roche," Fang said. "Safety is always key—it can protect the operator from the running turret when adjustment is necessary."

In addition to the isolator, Shanghai Roche also installed PSL's ChargePoint split butterfly valves, which allow contained transfer of highly potent sample and reject tablets. The valves comprise two parts: an "active" half that connects to the tablet press and a "passive" half that connects to a container. The passive half docks into the active half and is secured by turning a locking ring. When the valve opens, tablets transfer from the press to the container without exceeding an IOEL of 0.01 mg/m³. When transfer is complete, the valve closes by moving the handle clockwise. Then the locking ring can be released and the passive valve can be undocked.

"We installed ChargePoints in the press's reject port and the sampling port, as well as in the reject port of the metal checker," Fang said. "From Roche's side, this equipment was very



Split butterfly valves allow safe tablet sampling and transfer.

important, especially the sampling port, because we have no online weight checking so we need to take samples. The containment of the sampling process became a key point for us." While Shanghai Roche is still verifying the containment performance of the isolator and the valves, Fang is confident the installation will meet its objectives. "We have been successful on all measures," he said. The company has conducted installation qualification and operational qualification that satisfied its internal guidelines. Test results on actual IOELs are due soon, and Fang predicts the company will reach its goal of 0.01 mg/m³.

Even before the final numbers are in, however, Fang said he is happy with the project. "PSL is a good choice for the reform or modification of old equipment for containment production. The employees' professional attitude during installation and the company's equipment definitely satisfied us."

In March, Shanghai Roche's high-potency facility won the Facility of the Year Award for product execution regional excellence. T&C

Powder Systems, Boise, ID.

Tel. 208 376 7008

Fax 208 376 7999

Website: www.powdersystems.com