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Meeting Challenges in Desiccant Dispensing

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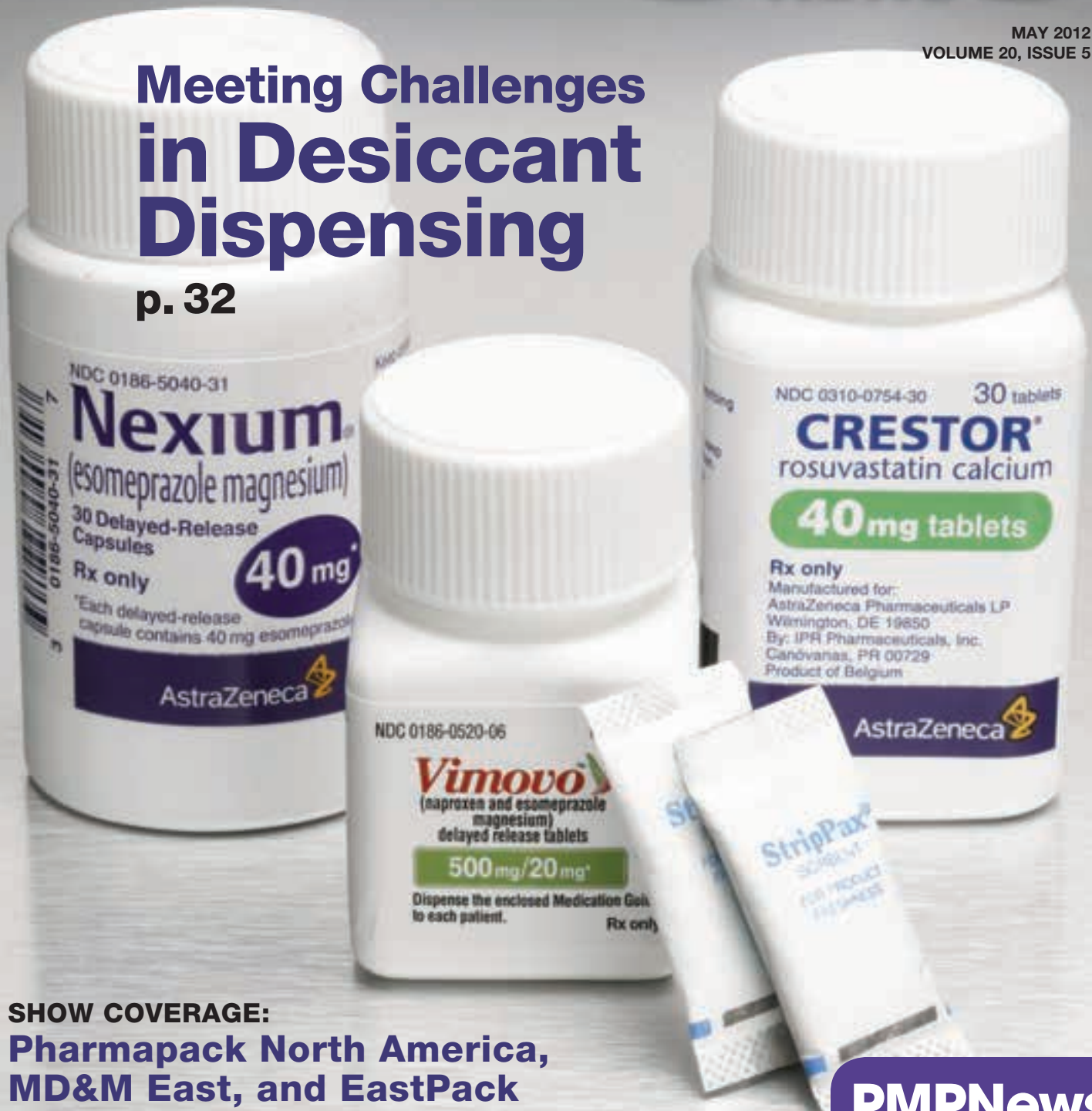

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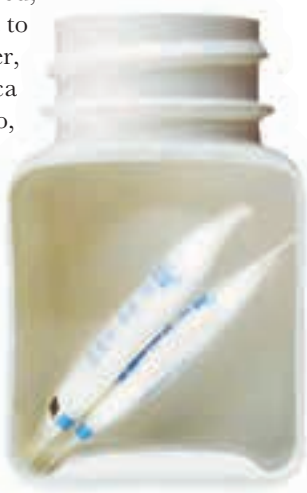
Meeting Technical Challenges in Desiccant Dispensing

AstraZeneca increases efficiency and prevents scrap with Multisorb's StripPax System.

Christopher Garrod knew he would need a desiccant in his sample bottles of Vimovo, but after speaking with his R&D team, Garrod, a senior engineer on the Packaging Process Execution Team for AstraZeneca, immediately realized it would present a unique challenge. Vimovo, a fixed-dose combination of enteric-coated naproxen and immediate release esomeprazole, is a highly moisture sensitive drug. The atmospheric exposure limits for the desiccant were a lot tighter than any product they had packaged before, presenting Garrod with his first challenge.

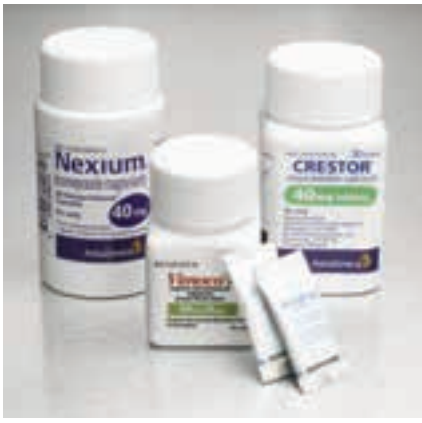
PACKET OR CANISTER

Choosing whether to use a packet or canister desiccant became clear to Garrod early on in the process. AstraZeneca was currently using desiccant canisters in its tablet packaging where it was required, so using canisters seemed at first to be the obvious choice. However, at the same time AstraZeneca was preparing to launch Vimovo, it was also preparing to launch a product in Sweden called Axanum, a combination low-dose aspirin and esomeprazole tablet. During a transit study for Axanum, the capsules were physically damaged by the hard canister pounding against the tablets in the bottle.



Multisorb provided AstraZeneca with the StripPax Packet optimized to the drug product and packaging configuration.

Garrod, not wanting to take the risk that a canister might damage Vimovo in transit, felt his only options would be to use a canister with cotton fill, which would protect the tablets, or to use a desiccant packet system. According to Garrod, a cottoner can add complexity to the line, potentially creating efficiency loss as well.

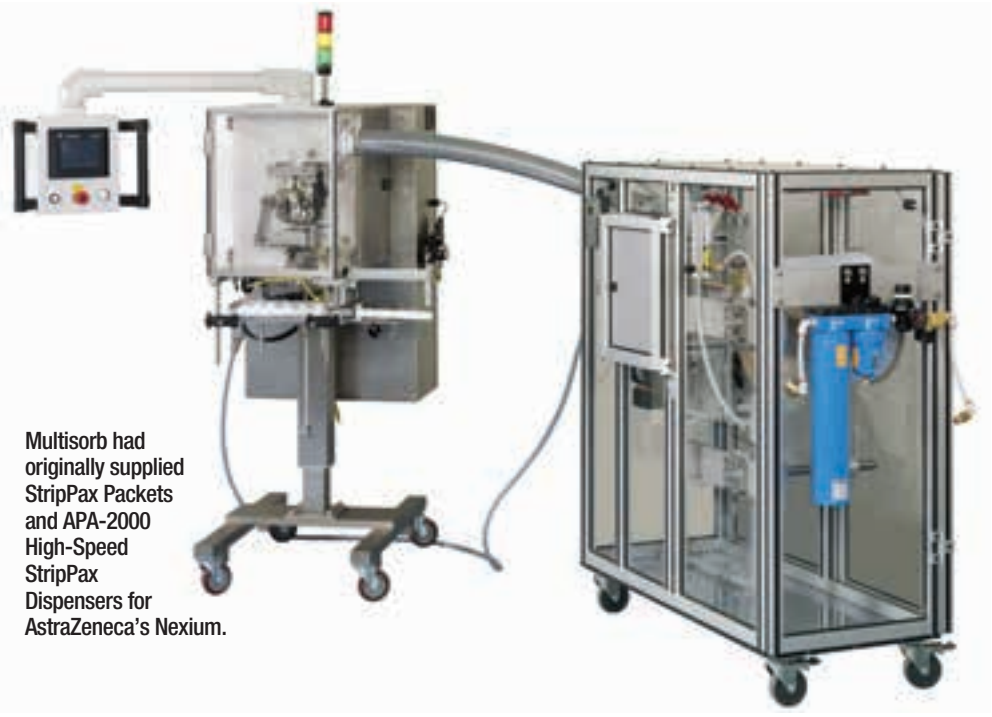


A greater concern, however, was that a canister desiccant might not be able to meet the tight atmospheric requirements of the Vimovo package and bottling operation. Canisters are typically loaded into a hopper that is exposed to the packaging room's environmental conditions. Because the desiccant required for Vimovo had a short exposure time during the commercial packaging operation, the canister would quickly become overexposed, leaving them with less than the required capacity to maintain the stability of Vimovo throughout its shelf life. These obstacles turned him away from canisters and solidified his decision to use packets.

"We looked at how much rework and how much desiccant we would have to throw away from an operations standpoint if we went with canisters. We had really tight operational requirements and we knew we would be disposing of canisters because we couldn't run them fast enough," said Garrod. For increased run-time efficiency and cost savings in terms of limiting scrap, using a packet type desiccant became the only option for AstraZeneca.

IT CAN'T BE DONE . . . OR CAN IT?

In addition to the tight exposure limits, the bottle was small, a 45-cm^3 bottle with an inner diameter opening of approximately 20 mm. Additionally, the chemical stability requirements of Vimovo required that two one-gram



Multisorb had originally supplied StripPax Packets and APA-2000 High-Speed StripPax Dispensers for AstraZeneca's Nexium.

desiccant packets be inserted in the bottle at a high speed. Garrod contacted his current canister supplier, but was told that it wasn't possible to do with desiccant packets.

AstraZeneca relied on corporate networking to find a supplier that could provide the desiccant packet and dispensing machinery. It turned to its machinery integrator for a reference, who recommended Multisorb Technologies. AstraZeneca, however, couldn't rely on the recommendation from only one source, so exercising due diligence, it sought references from another pharmaceutical company, who also revealed a positive experience working with Multisorb.

"To hear the integrator and then another customer speak highly of Multisorb was a big plus for us," said Garrod. He decided they needed to bring Multisorb in and take a closer look at their capabilities.

UP FOR THE CHALLENGE

A meeting was set up between AstraZeneca and Multisorb. Multisorb presented its StripPax System, which includes a StripPax Packet that is optimized to the drug product packaging configuration and a StripPax Dispenser. The StripPax Packets are compact, non-dusting packets that are accurately inserted into the bottles at a high speed. The StripPax Dispensers are available in low-, mid-, and high-speed designs with a variety of options; they are designed to operate seamlessly with a variety of packaging lines. Because the StripPax Dispenser is designed to run exclusively with the StripPax Packets, downtime is minimized. With a typical bottling operation, this would be a turnkey solution for pharmaceutical packagers. However, AstraZeneca had a unique challenge that would require some modifications, but Multisorb's team was confident they could handle it.

"We had a technical challenge and Multisorb was the only company that could provide a solution. We looked at other suppliers and they came back and told us they couldn't do what we needed," explained Garrod. "Multisorb was the only choice for us."

The relationship between AstraZeneca's Vimovo team and Multisorb was solidified. As it turned out, Multisorb had supplied the StripPax System (StripPax Packets and APA-2000 High-Speed StripPax Dispensers) for the packaging of AstraZeneca's Nexium (esomeprazole magnesium tablets) for the North American market. However, Nexium is manufactured and packaged by Merck & Co. as the result of a joint venture between Astra and Merck in the 1990s, so the Vimovo team wasn't fully aware of this relationship.

ONE SIZE DOES NOT FIT ALL

The APA-4000 Twin-Head, High-Speed StripPax Dispenser purchased by AstraZeneca as part of the StripPax System featured an optional containment system with dry air purge. The packets are never exposed to the ambient atmosphere, ensuring that they always retain the specified capacity to positively contribute to the stability profile of the drug product as intended. This satisfied the requirements for AstraZeneca's environmental exposure limits.

Additionally, the dual-head dispensing from the APA-4000 StripPax Dispenser made it easy for AstraZeneca's speed requirements to be met.

For increased run-time efficiency and limited scrap, using a packet became the only option.

The challenge of the small sample bottles would be slightly more difficult, but Multisorb's technical team was ready to take it on. The small bottle would be required to hold two one-gram packets. Physically the height and width of their typical packets were too large to fit even one packet into the bottle, much less two. A new packet design would be required.

Multisorb's technical team worked closely with AstraZeneca to meet their specifications. With its comprehensive

knowledge of desiccants, they were able to reduce the physical dimensions of the packet. The new packets fit through the mouth of the bottle with only a few millimeters clearance. With the precision placement of the APA-4000, this was more than sufficient clearance.

FACTORY ACCEPTANCE AND VALIDATION TESTING

AstraZeneca was so pleased with Multisorb that it purchased two systems. Along with the APA-4000 they purchased an APA-2000 High-Speed StripPax Dispenser that would eventually be used on another line for a product that was still in the regulatory approval stage. AstraZeneca required factory acceptance testing (FAT) prior to receiving and installing the machines. The intricacies of the APA-4000 FAT created a learning experience for both parties, but Multisorb was able to meet all of AstraZeneca's requirements. The APA-2000 FAT ran without a hitch, also meeting all of AstraZeneca's requirements, and both dispensers were sent to AstraZeneca's packaging facility in Newark, DE.

Once the APA-4000 dispenser was installed on the line, Installation Qualification, Operational Qualification (IQ/OQ) validation of the machine was performed. The IQ/OQ validation went very well, and the first commercial purchase order was run.

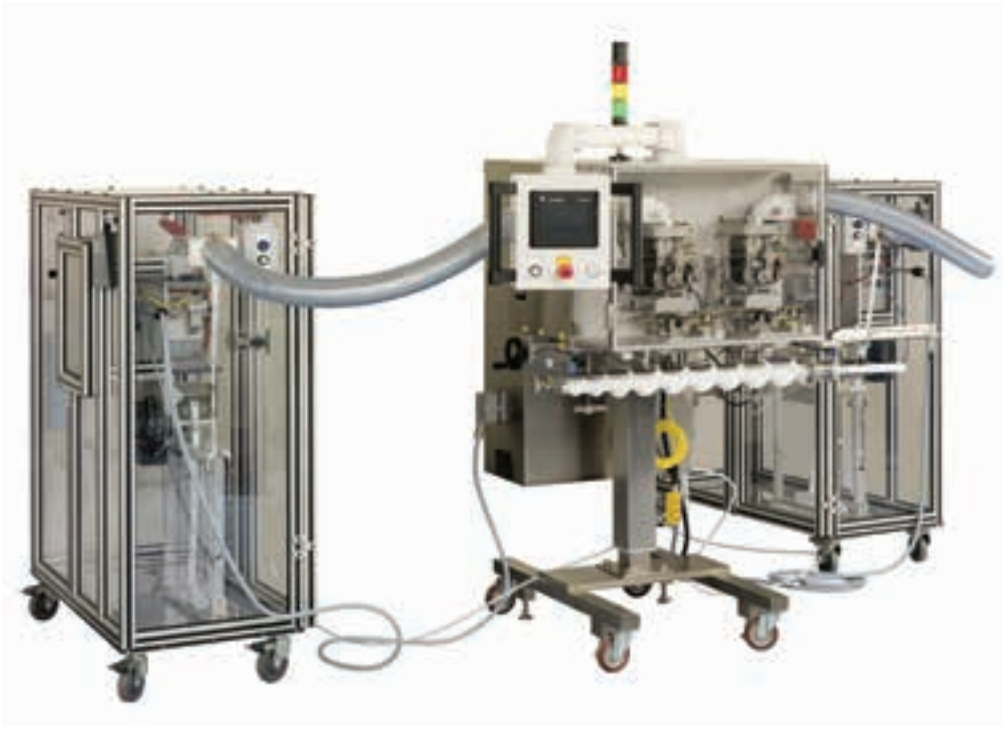
"The first time you bring anything online, everyone is nervous. But the first commercial P.O. ran really well," remarked Garrod.

CONTINUING SUPPORT

The uniqueness of the double-drop placement in the 45-cm³ bottle presented new opportunities for creative collaboration between Multisorb and AstraZeneca. Ideally, the first packet should drop into the bottle and fall into a horizontal position. At times, however, the first packet would drop in and remain vertical, preventing the second packet from entering the bottle properly and causing it to bounce out. A dispenser design addition and setup modifications had the line running smoothly once again.

The partnership between Multisorb and AstraZeneca remains strong. AstraZeneca, working closely with Multisorb, often takes a proactive approach and will anticipate and rectify a situation before anything can become an issue on the line.

Garrod explains: "We work together to figure out how to prevent potential issues. It is definitely a collaborative effort. It isn't us making changes on our own or Multisorb telling us to make changes. It has been a joint effort to get where we are."



Packets are never exposed to the ambient atmosphere in the APA-4000 Twin-Head, High-Speed StripPax Dispenser, maintaining their specified capacity.

Since the initial challenges were overcome, the efficiency and reliability of the dispenser has been very good, according to Garrod. The packaging line is currently operating beyond its normal capacity in order to support product launches outside the U.S. market.

MOVING FORWARD

AstraZeneca has been so pleased with Multisorb's StripPax System that it has ordered two more APA-2000s to run Crestor (rosuvastatin calcium tablets), a drug product used for the treatment of dyslipidaemia. In the previous packaging operation in Puerto Rico, the tablets were packaged with a canister desiccant. When the products transfer to Newark, DE, the canisters will be converted to the StripPax System. Multisorb's R&D team worked with AstraZeneca to do equivalency testing on the StripPax Packets to prove that there would be no impact on the drug product integrity with the switch.

"Buying four machines demonstrates that I am very happy with the StripPax System and the great service I receive from Multisorb. We have created a mutually beneficial and collaborative relationship. When I call, I don't even have to say my last name; they know who I am," Garrod remarked. ■