Nothing to Sneeze At

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Sneezing, coughing, congestion, itchy eyes — we've all had these symptoms at one time or another. Most of the time, these symptoms are attributable to seasonal allergies, but what do you do if the popular over-the-counter remedies don't relieve them?

Many times your next step would be to go to an allergist or immunologist who would perform a series of tests to determine what is specifically causing your symptoms. These specialists rely on the products manufactured by companies like Allergy Laboratories, Inc. (Allergy Labs) in Oklahoma City, OK.

Allergy Labs is an FDA-licensed cGMP pharmaceutical manufacturer of over 500 different biological allergenic extracts for the diagnostic testing and therapeutic treatment of allergies via subcutaneous injection. The company also provides sterile depyrogenated vials and sterile diluents, which are also manufactured at the Oklahoma City facility on fully automated lines. The company's contract manufacturing group custom fills, private labels, packages and manages a wide inventory of vial sizes and fill volumes of diluent.

The company had been operating a very successful and fully operational line when, in 2008, the decision was made to expand operations to a second filling line. To determine exactly what needed to be done and put a plan in place, Warren Johnson, vice president and co-owner (with wife Rebecca), invited Bruce Anthenat, president of AWS Bio-Pharma Technologies, for a site visit to discuss unique and cost-effective ways to help him expand the business. Together, Allergy and AWS Bio-Pharma

established the project parameters and performed pre-engineering activities. The primary goals for the facility expansion were:

- A new parenteral processing facility using modern design methods, state-of-the-art equipment and executed in a cost-effective manner.
- Expanded warehouse/storage capabilities.
- Initial production of injectable products (SVP) in 12 vial sizes from 2 through 100 cc.
- One high-speed production line with the potential to add a lyophilizer (in the future).
- Primary production facility for Allergy's larger batch sizes (up to 700 liters).
- Production of up to 400 VPM of 2-cc vials
- Production of up to 200 VPM of 10-cc vials (a rather difficult to handle vial).
- Production of up to 30 VPM of 100-cc vials.
- A location on the existing employee parking lot (as the existing parking lot was moved).
- No interference of the expanded construction with the daily operations of the existing facility.
- Sizing of all new utilities (plant and critical) to accommodate the existing facility.
- Cost of the new facility (building, utilities and processing equipment) to fit within the owner's budget.
- Startup with existing products under the control of Allergy Labs.
- Additional capacity for new contract manufacturing opportunities.
- A state-of-the-art finished project with FDA and EMEA acceptance.

The resultant 13,000 SF expansion of the existing facility meets the company's current and future needs.

Background

In essence, Allergy Labs operates as two companies — as Rebecca Johnson, DPh, President and co-owner explains, "The allergy or biological products we make are

FDA-licensed products. Allergy Labs was founded as an allergenic extract company in 1929. We manufacture concentrated allergenic extracts using biological source materials, including pollens, molds and foods for diagnostic testing. These same extracts are also used to compound customized diluted mixtures formulated for a patient's specific allergies. In other words, these drugs are used for allergy immunotherapy, desensitization, and many people call them "allergy shots."

And as Warren Johnson explains, "This company has always manufactured diluting solutions and sterile empty vials to assist physicians with their allergy compounding needs. We also support our competitors by private labeling many of their allergy products. When my wife, Rebecca, and I bought the company 10 years ago, 'private labeling' was what this service was referred to as, although it was certainly contract manufacturing and thus initiated our decision to expand out of the allergy sector into other injectable products. We manufacture injectable vasodilators, vasoconstrictors, a few CNS (central nervous system) drugs for which the trade name drug has come off patent. We perform the necessary validations, exhibit batches — the customer does the ANDA filing, and once FDA approved, we are 'off to the races'."

Two Different Sources — One Final Destination

As mentioned, the company can make over 500 different allergenic extracts for allergy testing and treatment. These biologicals are extracted in a glycerin solution and go through a multi-step intense filtration process to move the solution from coarse to sterile filters and finally into sterile, multi-dose vials. For the contract manufacturing portion of the business, the company obtains the active pharmaceutical ingredient (API), formulates the drug batch solution and fills into sterile vials aseptically.

On the continuous fill line, vials travel through a vial washer, depyrogenation tunnel then to the filler, stopper and capper equipment. It is not until after they have a sealed finished vial before the vials are handled for inspection. This process significantly reduces the risk of contamination.

When the company decided to expand its production facilities they wanted to duplicate the success they had with the existing line one on the new line (line two) in their new facility — but with enhancements as new technology would allow. As Lee Beaver, the company's director of manufacturing explains, they looked at several new technologies and decided to incorporate those they thought would provide the most benefits.

In particular, some of the new barrier isolation technologies were considered, but not implemented. "We considered using other technologies — but based on our experience with line one, which we've had great success with, we wanted to mimic that success in line two. We definitely improved the manufacturing in some areas on line two by implementing more operator/product barriers and particularly in the area of less product handling. We used conveyor systems and accumulation tables to move product from one area to the next as opposed to manually traying vials and physically carrying them to another machine.

“As far as aseptic filling is concerned, isolator and restricted access barrier system (RABS) technology is out there, and some companies use them, but the cons outnumbered the pros when considering implementing these technologies into our operation. Setup and sanitization procedures for these isolation or barrier systems would increase changeover time from one vial size to the next. Our operation can require daily vial size changeovers and that lost time is critical to us.”

As far as the changeovers go, the company does do it often, “There are approximately 15 different vial sizes we aseptically fill and assemble. Some customers want a 2-mL fill in two or three different vial sizes, and some request multiple fill volumes in the same size of vial. When providing contract manufacturing services, we have to be equipped to handle these special customer requests. Therefore, there is a vast array of vial sizes that we have to have our machines specifically made to handle.”

Having so many different vials to fill puts a large emphasis on the equipment vendors and the machinery they supply. But as Beaver says, it’s really a two-way street, “We rely on them a great deal. We, as the customer, supply them with our functional specifications: Here’s what we want to do — we want to handle these vial sizes at these speeds to meet our needs. They come back and tell us well yes we can or no we can’t. We don’t want to tell them how to make the machine because they are the specialists. They know their machine.

“We seek out and research equipment vendors, supply them with our specifications to determine what they can or cannot meet, narrow the field down to one, and let them build the machine. We rely on their expertise a great deal but at the same time we have specifications that we have to meet — but it’s definitely a partnership.”

One of the key features of the new expansion is how it was designed around a cleanroom “core” that was built with modular construction. Constructed in Italy, then shipped to the company’s site, the smooth installation and qualification of the clean room was a significant factor in the project’s success.

Smooth Construction

As anyone who has ever done any renovation or building project knows — problems do crop up. But for Allergy Labs and their facility expansion — any problems were kept to the bare minimum. In fact the facility expansion was completed ahead of schedule and under budget.

Johnson explains some of the reasons this project went off so smoothly. “The first reason it went well was that this was our third expansion, and although the first two did not include aseptic manufacturing space, we knew exactly what we needed in the aseptic area. The second reason is that I was actively involved in the day-to-day construction process, being more of a construction manager I suppose. Although some of my staff also helped in the planning processes, we were not held up for committee meetings, as I was always present to make necessary decisions to keep things moving swiftly. The third reason is that this project was started right at the economic downturn, so the contractors were available and always here on the job. We didn’t lose any time waiting.”

Director of Manufacturing Beaver echoes Johnson’s comments: “There really weren’t a lot of problems with the current production, manufacturing or scheduling during construction. Our original building contains line one, and the new building is separate and incorporates line two. Perhaps the biggest issue was warehousing as we needed access to building two to store items for building one."

Johnson adds. “There were some logistics issues that we had to work around. We had some temporary pads so that we could get in and out of our warehouse. The new building wraps around the old warehouse. But there was no interruption in manufacturing. In fact, we couldn’t have done this if we had any interruption in manufacturing. It just would not have worked.”

More Construction on the Horizon

Not content to rest on their laurels, the company is already looking towards another expansion project, as Johnson details. “We are planning a new 35,000-square-foot expansion that will house a new shipping and receiving area. It will have new quarantine warehouse space, released product warehouse space and a large area that is set aside for future aseptic manufacturing, but that will be for the future as we still have a lot of capacity in the current building.”

He continues, “We need more space for another labeling area, and we need space for shipping docks as well. Shipping and receiving is currently rather small — but we do have some interests from some of our current customers to begin distributing their product — but that will be further in the future, so that area will be in

anticipation of that possible future business."

The Best Part

The folks at Allergy Labs are justifiably proud of what they have accomplished, especially considering the project was completed under budget and ahead of deadline. As Beaver points out, "I come from the quality assurance side, the validation side. Warren gave us a deadline to meet and I'm most proud of meeting that deadline with our staff. We worked hard — we validated the entire line in six months after construction was complete.

Johnson concurs, "I have to agree with Lee. I come from the production side and what they accomplished is fantastic. For me — I really like the design. We didn't have much space. When we started this project we were hemmed in. We didn't have much land. It just so happens that after building two was built, the owner of the adjacent property finally agreed to sell — then the other properties also fell like dominos (not literally). So now we own the entire block, about 5 acres, whereas we used to own about 1 acre. When we originally bought this company in 2001, we only had about 40,000 square feet and that included our parking lot.

"We built this nice facility to run 3 shifts — 24/7 — and we did a great job of fitting a large amount of usable space into a small footprint."

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