
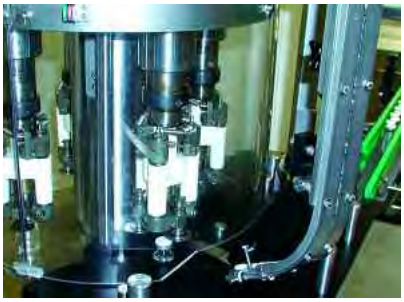


IG MANUFACTURING: UP CLOSE AND PERSONAL

Editor's note: While the following is a personal account of a tour that Kris McFalls took last fall at Talecris Biotherapeutics, please keep in mind that all manufacturers must follow the same stringent FDA guidelines for sterility and safety. According to Kris, "Taking this tour gave me comfort seeing firsthand the care and pride put into manufacturing the lifesaving medication that so many of our readers rely on."

By Kris McFalls

Last September, I visited Talecris Biotherapeutics' manufacturing plant in Clayton, N.C., for its third annual Up Close and Personal Patient Open House event—a plant tour that Talecris sponsors each year to give patients (even those who use competitors' products) a chance to see how and where Talecris' intravenous immune globulin (IVIG) and other plasma products are made. Altogether, there were about 50 of us visitors. During our two days there, we saw various parts of the manufacturing process up close, as tour participants were able to choose from one of five available tours (see the sidebar on Page 27 for an overview of the other tours). What follows is an account of my tour through the sterile filling facility, which provides final container filling, freeze-drying and pasteurization as appropriate for each product.

THE LOCKER ROOMS

My tour began with a trip to the women's locker room, as viewing the sterile filling stations required donning freshly cleaned scrubs that were ready and waiting, individually packaged neatly in plastic wrapping. Each bin of wrapped scrubs was labeled small, medium and large, but there was no tall or short. As a consequence, with my 5-foot-9-inch

frame, my scrubs barely reached my ankles. My friend, Gail Moore, a Talecris patient advocate who stands at least 6 feet tall, looked as if she was wearing capri pants, if not long shorts. Donned in scrubs and shoe covers, we were ready to enter the handwash room.

In the handwash room, we rejoined the men of our tour. Everyone was asked to wash hands and directed to grab a set of clean, individually packaged green coveralls. From there we entered a smaller empty room that functioned as a transition area called an airlock. By definition, an airlock is a compartment connecting two different environments that enables personnel to pass from one environment to another. Before opening the next door, the first door had to be completely shut or an alarm would sound.

Leaving the airlock, we entered another locker room, which gave me flashbacks of an operating room due to the sterile smell, the stainless steel environment and the cold temperatures. As I was imagining the next step to be an anesthesiologist with needles and a gas mask, we were asked to slip on hair netting, the green coveralls we were given, and gloves. A stainless steel bench marked a boundary that, once crossed, was considered "the clean area." Before stepping over the boundary, we sat on the bench and covered our feet with yet another layer of packaged booties. With every inch of skin from our neck down covered, it was time to address the face. Our eyes were covered with goggles, our mouths with surgical masks. The last step before entering the door to the sterile bottling area was to rub our gloved hands with antibacterial foam.

Once through the next door, everyone looked the same—green-clad androids. Some were taller, some were wider, but those were the only distinctions. I imagine working in that kind of environment would make you very good at reading another's eyes, as that is all you could see.

THE BOTTLING AREA

Loaded on pallets, the bottles come into this area by the thousands. Each bottle is placed in automated machinery that thoroughly washes and sterilizes it. After this, the bottles are lined up in a single line, like soldiers on a conveyor belt, ready for inspection. Each bottle passes through an inspection hood where any flaw is magnified, making it easy for the sergeant, uh, I mean, inspector, to identify any that need to be weeded out from the ranks. Each glass

bottle is automatically spun around to make sure every millimeter of its surface is examined. To ensure acuity and attention, the inspector—another green-clad body sitting with his or her head resting about a foot behind the magnified viewing glass—is rotated out every 30 minutes. ➢

THE FILLING AREA

The filling area consists of more rooms built with stainless steel walls and viewing areas that are enclosed in glass. As far as I could tell, the air in these rooms is about as clean as you can find. Only employees who work in these rooms can enter them. And when they do, they look like astronauts walking on the moon or investigators dressed in hazmat clothes at a crime scene. From their moon boots to their head covering, face shields and goggles, every inch of skin is covered. The sterile bubble-like work environment sparked memories of David Vetter, the boy with severe combined immune deficiency syndrome (SCIDS) who was raised in a bubble to protect his very fragile immune system. Apparently I was not the only one feeling this way, as Gail remarked, "They work in a bubble so we don't have to live in one." Another patient asked about the employees' needs for breaks. We were told every time a break is needed, the employee has to go through the entire gowning process from the start. Our tour guide reported this could happen several times a day.

I observed one worker in the bubble taking culture samples on every surface imaginable. Each sample was meticulously documented. Samples were taken multiple times throughout the day, seven days a week, 24 hours a day. I would imagine if you were an immune-deficient patient, this would be the safest place in the world to work.

Along the lines of safety precautions, if an employee reports to work with even an inkling of being sick (or having been exposed to a contagious agent), he or she must first report to the health center to be cleared to work in any of the sterile or clean environments. If there is any question, the worker will be reassigned to another area until deemed healthy.

After touring the sterile filling and bottling area, we reversed the process of gowning so we could get back into our street clothes. Having become so acutely aware of the clean and sterile environment, I felt as if I needed to treat my street clothes

with antibacterial spray before putting them back on.

Our tour over, our group was guided into the large company cafeteria. There waiting, as if a celebrity were about to grace their presence, were hundreds of Talecris employees who eagerly wanted to hear from us how what they do affected our lives. They listened intently as Tyler from Chico, Calif., told them how much of his first two years of life was spent in a hospital with multiple bouts of pneumonia. Tyler went on to say that because of the love and support of his mom, as well as his IG therapy, he not only survived the near-death experiences, but also thrived. Today, he awaits acceptance into medical school. Another gentleman got up and thanked the employees for allowing him to be bored and eat cottage cheese. Before his diagnosis of alpha-1 antitrypsin deficiency (genetic emphysema), he was near death, unable to eat or breathe unaided.

After absorbing all the patient testimonials, many employees thanked us for showing them how important their jobs are. As the meeting concluded, the many hugs exchanged were not unlike those seen at the end of a family reunion. ◪

OPEN HOUSE PLANT TOURS

The following five tours are available at the Open House[1]

IVIG-C Facility

This manufacturing facility is solely dedicated to the production of Talecris' intravenous immune globulin therapy. (The C refers to caprylate/chromatography purified.) The completely closed and highly automated production process involves a series of pathogen reduction and product purification steps. The facility includes two identical production lines, called "trains," that can process two batches of IGIV-C independently. The tour is conducted in a corridor adjacent to the manufacturing area and includes a detailed description of the facility and the production process as well as an opportunity to watch as employees utilize various stainless steel vessels, filter presses, chromatography columns and ultra-filtration systems to manufacture IGIV-C.

Packaging and Shipping Facilities

Tour participants watch as the packaging team handles the incubation, cold storage, staging, inspection, label development and packaging of all products. They will then follow the products to the shipping facility to view product shipments, which are packed in special shippers that control product temperature and maintain product integrity. Talecris' innovative packaging and shipping solutions provide the final link in ensuring product safety.

Alpha-1 MP Facility

The Alpha-1 Modified Process (MP) facility is dedicated to the production of Talecris' next-generation Alpha-1 therapy, which is currently in the clinical trial phase, for Alpha-1 Antitrypsin Deficiency (genetic emphysema). The brand-new facility incorporates technology changes into the current manufacturing process. The modified process also includes additional viral inactivation/removal steps, such as nanofiltration. A tour of this facility includes a detailed description of the facility and the production process as well as an opportunity to see the purification columns, ultrafiltration skids, vessels and computer control systems that are used together to produce Alpha-1 MP.

Sterile Filling Facility

The sterile filling facility is dedicated to aseptic, contamination-free bottle filling and provides final container filling, freeze-drying and pasteurization as appropriate for each Talecris product. Anything that could potentially affect product sterility must be strictly controlled during the filling process. Therefore, every detail of the facility is designed to eliminate points of potential contamination. Tour participants will watch as primary aseptic filling occurs on four filling lines that represent the highest clean room standards. These lines handle glass vials ranging from three to 250 milliliters.

Fractionation Facility

Fractionation is the complex process of extracting delicate proteins from human blood plasma for the manufacture of a variety of intravenous and intramuscular therapeutic biological products. Multiple steps using controlled agitation, temperature, ethanol concentration and variation in pH are involved in isolating the proteins into fractions. Tour participants will watch as frozen blood plasma is removed from containers using an automated bottle opener; combined and thawed in large vessels; and processed using Sharples centrifuges, Schenk filter presses, 6000-liter tanks and acetone drying.

[1] The following descriptions were taken from informational brochures about the Open House and were printed with the permission of Talecris.