

JEFFREY BUGULISKIS: Welcome to GENcast, a sponsored podcast series brought to you by *Genetic Engineering & Biotechnology News*. I am your host, Jeff Buguliskis.

It is a wondrous sight to see a seedling begin to burst through the topsoil. That faint green hue in its gritty black and brown surroundings, what will it become? A beautiful flower? A delicious vegetable, perhaps. Whatever destiny lie ahead for that new member of the plant kingdom, it is important to note that its fate is inextricably linked to aid from the surrounding environment, like the rain, sun and even the soil conditions.

In many ways, science is the same as the budding plant. It needs to be cultivated as scientists rely on each other for assistance and guidance to move their research and the field forward. Emerging scientific markets -- like China, for instance -- are especially sensitive to those surrounding environments, while at the same time driving the need for greater flexibility for scaled-up biomanufacturing facilities.

Now, much like how the nourishing rains and sunlight help our little seedling, the M Lab Collaboration Centers

at Merck support the mission of China's fast-paced, future-looking biopharma market with skilled knowledge and training.

The M Labs have built a global network of expertise that makes it easy for researchers in key biotech hubs around the world to explore, learn and collaborate in order to solve some of the toughest problems in the life sciences industry.

I chatted recently with three M Lab team members to hear how they tackled some recent customer challenges. Let us meet them, shall we?

DANNY WU: My name is Danny Wu. I am based in Beijing, and my title is Senior Biomanufacturing Engineer Manager, focused on chromatography technology.

EVAN WONG: I am Evan Wong. I am a process development scientist manager from M13, and I am based in Shanghai, China.

MATT TURIANO: I am Matt Turiano. I am a biomanufacturing engineer in Burlington, Massachusetts, in the USA.

JEFFREY BUGULISKIS: Let us start by talking about the M Lab Collaboration Center in Shanghai. What makes it unique, and how does it address customer needs in the fast-paced Chinese biopharma market?

DANNY WU: Okay, fantastic question. So, in terms of M Lab, you know, M Lab was launched in Shanghai, and is a big central city. Now, here the driving the main biopharma industry in China is currently for monoclonal antibodies.

And Shanghai M Lab has a high throughput process development platform for chromatography technology. And a manufacturer can have had occurrence with chromatography technology in the Shanghai M Lab. How do you think, Evan? Do you have any other ideas for the M Lab?

EVAN WONG: Yeah. Our M Lab is a flexible, non-GMP environment lab center. And here, scientists and engineers can collaborate with our technical experts to solve problems without interrupting their own production. And the manufacturers can have hands-on experience with single-use technologies and all other products or systems.

To expand upon that, my next question would be, what kind of challenges are customers bringing into the M Lab in China?

DANNY WU: Yeah, it is a good question. Yes, you know, there really sometimes are challenges for different technology. And let me focus on a specific challenge today about the chromatography technology. You know, in this case, it is about that the manufacturer had concerns about the short lifetime of chromatography resins.

They only get 80 cycles for chromatography affinity resin lifetime in that process. So, this is why we bring them into M Lab. You know, the manufacturer had a limited occurrence with chromatography technology. It is currently how to do clinical validation on lifetime studies for resins.

And they were on a short timeline. They only had one and a half months to find good cleaning buffers and draw the lifetime scaled-down model. They were facing facility as well as technology constraints with chromatography.

EVAN WONG: I think it is great, Danny, for your case. This is very challenging for a customer. I also experienced a lot of challenges from customers, you know, accept process developing work in the M Lab, where also it is a lot of application case.

One of my experiences with that, the first mAb company that is happening in China, they want to set up 1,000-liter single-use upstream line in their standing-still facility.

So, the manufacturer actually had limited experience with single-use technology. They were on a short timeline. This project needed to be up and running within four months to submit the application to the SFDA (State Food and Drug Administration) on time. That means they needed to start the production when they received our single-use system.

And they were also facing facility constraints with SKR. There was only a half meter left for the ceiling to install the 1,000 liter single-use bags.

JEFFREY BUGULISKIS: How was that manufacturer's problem solved?

DANNY WU: Yes. We solved the customer's problems. But the other two solved the manufacturer's problems. They performed cleaning buffer optimization with a high-throughput process development platform and found the good buffer for the resin cleaning.

The team at M Lab showed the manufacturer how to find the optimized cleaning buffers and how to do a lifetime study with a scaled-down model. And we worked with the customer to achieve 150 cycles lifetime for chromatography of finish resins with optimized cleaning buffers.

The work done in the M Lab allowed the manufacturer to increase lifetime of their chromatography resins because of the cleaning buffers. They were then able to apply this new process to successful therapeutic production for their clinical trials.

EVAN WONG: Oh, Danny, it is really a great job you have done. I think we have another solution for our customers with single-use technology. You know, another

advantage of M Lab is we can do the demos, work around or even process simulation according to customer process.

We perform demos by using a 200-liter single-use bioreactor so that our customer could have hands-on experience with the technology and get familiar with the stuff well and the residue setting. And even more, the team at the M Lab showed the customer how to design their single-use process using its bags and assemblings. Then the customer could simulate their process for medium preparation to cell culture and harvest.

And we also worked with this customer to find the solution for the installation of a 1,000-liter bioreactor despite the facility's space constraints. And in order to make sure the customer had the real experience of 1,000-liter bioreactor operation, we also took them to the North American M Lab to operate the 1,000-liter bioreactor.

You know, there are -- there nine M Labs Collaboration Center worldwide. So, we can share the results between each region, if they can help the customer to solve his problem. I think Matt can have -- speak on the demo in the North America M Lab.

Finally, the work done in the M Lab allowed the manufacturer to make the transition from the standing still to single use in their upstream process.

MATT TURIANO: Yeah, thanks, Evan. That is a great segue into talking about the strengths of our global M Lab network. We had a piece of equipment here in Burlington in the U.S. that we did not have in another location, and the customer was able to come to us here and to really get the full experience of using all of our equipment.

And we -- it was pretty routine for us in Burlington, just to set up a water run on the 1,000-liter bioreactor so that the customer could walk through all the way from the beginning, the physical bag installation and setup, along with kind of equipment management and really figuring out the spatial concerns that they had with that very large piece of equipment.

It is something that you do not -- you cannot quite get when you are not physically present with the equipment, to understand the size and scale and potential physical requirements of the operator using it.

So, you know, overall, the experiment went well. The customer was happy, and it really showed off the strengths of the flexibility of the global network and also all the capacities that we have at the Burlington site.

JEFFREY BUGULISKIS: So, how is the team at the M Lab preparing for the future of biopharma in China? What challenges lie ahead, and how are you anticipating them?

DANNY WU: Yes, we want to prepare something for our lab's future to support the manufacturer better. And we want to expand square footage facilities for M Lab, and also automation setting up in the M Lab. And they want to improve training capability for different applications in M Lab in the future, and to meet the biopharma market demands in China.

So, Evan, do you think these challenges -- what is the biggest challenge, and for us, how are we fixing them.

EVAN WONG: Yes, I think China's biopharma market is developing at a very fast pace. The diversity of the biopharma market requires to improve our training and the application capability in M Lab for different market segments, or different technologies, such as gene therapy, next-generation processing, single-use PAT, et cetera.

If we have this new application capability, we cover more customer needs. We can set up a very good relationship with customers. I think it is very fantastic.

JEFFREY BUGULISKIS: Evan, Danny, Matt, thanks very much for joining this discussion today, and thanks very much for your time.

Thanks for listening to GENcast. For *Genetic Engineering & Biotechnology News*, I am Jeff Buguliskis.

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