STARTING MATERIAL COLLECTION & OPTIMIZATION

CHANNEL CONTENT

Considerations for developing scalable and efficient collection network processes

Lacey Anderson, Sara Butler & Allison Montalvo

Many crucial considerations impact a cell and gene therapy developer's apheresis center selection strategy and ability to efficiently scale processes. Anytime collection processes or protocols differ from those in place at a center, there are likely implications for training, forms, and standard operating procedures (SOPs), which can potentially delay the first collection. In this panel discussion, three experts answer questions on apheresis center best practices within the allogeneic product collection pathway.

Elisa Manzotti, CEO, BioInsights, **speaks to**
From left to right: **Lacey Anderson,** Senior Manager, Collection Network Management, Be The Match BioTherapies, **Sara Butler,** Network Liaison, Be The Match BioTherapies, and **Allison Montalvo,** Program Manager, Oncology, Janssen (a division of J&J)

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Q How has COVID-19 changed the scalability landscape?

LA: COVID-19 has shown the need to have diversity within your collection network. COVID-19 highlighted the worst possible scenario for a lot of organizations. By having multiple locations and being adaptable and flexible, we had minimal disruptions in our collections as we moved through 2020 to 2021.

As COVID moved around the nation in waves, with hotspots in different areas, having multiple locations at our fingertips gave us the ability to shift collections and shift priorities to keep going forward.

Q Outside of processing requirements, what considerations may have a large impact on scalability?

LA: One of the largest considerations is the apheresis centers that are selected.

Apheresis center selection is key to growing a scalable and efficient collection network. When you are going through the process of identifying apheresis centers to participate, you need to ensure that the centers are able to grow and adapt through clinical trial changes.

Any clinical trial does not follow the exact same processes at the beginning in Phase 1 as they do closer to Phase 3. Things change, and through the course of the trial, different aspects of the process change. Having apheresis centers that are willing to grow with you and accommodate those changes is key to ensuring you are able to scale up further along in the trial.

AM: From an industry perspective, selecting apheresis centers that are open and willing to partner with you is very important. For young biotech companies, a lot of the challenges revolve around learning more about managing and standardizing processes. Being able to partner with an apheresis center allows for working together with the industry to drive standardization.

SB: The apheresis center selection is a huge consideration. The starting material, and the manufacture of that input, are also important considerations – where are things going? What kind of impact will that have on the process and vendor selection?

Q Is it a challenge to get a center to change its process to accommodate a protocol? If so, how would this be overcome?

AM: From my experience in a biotechnology environment, centers are always willing and open to working with their industrial partners. The responsibility is on the industry partner to make sure that they are not putting unreasonable expectations onto an apheresis center for a particular protocol change.

Apheresis centers are working with a lot of different clinical trial sponsors and each sponsor has a unique manufacturing process. They may have unique testing and product requirements, from fresh to cryopreserved process and shipping. These differences are opportunities for failure along a logistics process in cell and gene therapies.

You need a solid relationship in place to work with centers to understand their current process and experience. What is a must-have versus a nice-to-have? And what does that mean from a manufacturing perspective?

Despite centers being very willing to partner with industry, you must ensure that the must-haves are being fulfilled and that the industry is working together towards standardization. We are putting pressure on apheresis centers to be able to manage all these different individual unique requirements, resulting in a lot of staff training. That became a challenge during COVID, with staff being redirected to focus more on the COVID pandemic versus their normal roles. There is a lot of training that must go into this.

Centers also have a ton of standard operating procedures (SOPs) throughout manufacturing, so keeping an account of what we are asking of centers and where can we work to standardize is important. You have to know your process and your product – and work to educate the centers on why it's important for patients.

SB: That's a great point. A lot of these centers are on the end of the downstream, so all these changes happen, then it gets to the center, and it becomes a challenge. Making sure it's a partnership, and these sorts of challenges are discussed and decisions made upfront with the center is key. You need to think through the impact this will have downstream. Keep in mind, they are the experts.

Q Are there concerns with holding a product overnight for processing if a site has limited capacity?

LA: Many cell therapy labs don't have additional space to hold product for a long time, which is a challenge. Holding a product overnight for an early morning pick-up is absolutely something they can accommodate. However, when the product returns to the center for infusion after manufacturing, the packaging can often be bulky. Holding some of those materials tends to be more of a challenge for the apheresis centers unless they have built out additional capabilities. The addition of the shipping materials can be quite burdensome for long periods of time.

SB: There definitely are concerns with capacity and space. Once it has been processed, the storage, space, and timing are all considerations. There are always other things happening at the centers, and other protocols and sponsors to consider. The longer the product is held before being processed, the more of a concern it is in terms of product quality.

LA: When considering cells being held, there is a lot of data that manufacturing teams have to structure: how long hold times are, what temperature the cells are at, the stability of the cells, and how that would correspond to being a solid input.

With a cryopreserved product coming back, you need to make sure that your centers can manage and maintain that inventory. You need to be able to allocate resources to make sure that it's managed, held, documented, and tracked the right way.

There is a lot of effort in the upfront process when looking at different manufacturing hold times of fresh versus cryopreserved material. Considerations from the industry side include looking at your manufacturing process and logistics to have the data to determine what is an acceptable product inbound to your process.

Q What is the typical starting material?

SB: The typical starting material for us at Be The Match Biotherapies (BTMB) is mononuclear cell (MNC) collections. There are also some requests for hemopoietic progenitor cell (HPC) products, and the processing varies after that. The starting material that gets shipped is usually either fresh or concentrated and cryopreserved. We are getting a few requests for more complex processing, and as the industry grows I think we'll see that more, which is exciting.

Q What processing capabilities do sites have?

SB: Centers in our network all have the capability to collect fresh product and packaging shipments. Several of them also have the capability to concentrate and cryopreserve cells.

As the industry grows, and centers grow in their capabilities, we are seeing some in our network that can perform early manufacturing steps and more advanced processes such as selections and isolations. As sites and centers become more advanced, there are more protocols and opportunities for growth.

LA: We are seeing a shift in centers starting to build up capabilities. Four years ago, we did not see this as often. Now, we have a lot of centers who are asking what is it that we need to stay relevant, and how we can continue to assist and participate in the industry. We have seen a shift in the collection centers and their willingness to adapt and grow within the industry.

Q Which party decides what type of packaging is used for shipping?

LA: Often, the contract research organization (CRO) will have specifications for how they want to receive the product. However, with an open relationship and partnership, you can decide what is best for both the manufacturer and the apheresis center.

SB: Packaging is always a hot topic when looking at moving live cells around in a logistics supply chain area. Typically, the sponsor's responsibility is to design the packaging to make sure that they are sustaining the product throughout the lifecycle in a way that has data to support it. You always want to know what capabilities your center has. It is always good to talk about capabilities and typical packaging configuration within your questionnaire. You want to get that input early so you can look at the capabilities you are going to put around your product and try to streamline and standardize as best you can to site.

It comes back to risk in the supply chain. The more specialized and individual you become in your requirements, the higher the risk of failure within your process. To manage this, as a sponsor, we design the pack out. We know what requirements we have from maintaining cell viability, maintaining temperatures, where we are traveling and transporting from, and what qualities we need coming in. We design that, then we go out and talk to sponsors. We work with the BTMB team and the logistics center and we try to align with where the industry is moving and what the standards are. Typically, the sponsor is the person or group that is responsible for designing that.

Q Are there common product tests that are done at the sites?

SB: Complete blood counts (CBCs) and sterility are the tests that the sites are performing on a routine and standard basis. Some centers have also been asked to report flow testing results.

Q Within biotherapy or otherwise, what is the future of the collection network?

LA: For us at BTMB, we are focused on ensuring agility and versatility within our collection network. We know we need to be adaptable to shifts in the industry; for example, over the last four years, we have seen a shift from fresh MNC to more cryopreserved or peripheral blood mononuclear cells (PBMCs). As the industry grows and science and technology advance, our collection network needs to be ready to handle it. We want to be prepared and not have to build out those capabilities when requests come in.

For us, it is important to be agile and versatile, so that we can accommodate any of the processes that our sponsors have set up. We understand the commonalities in the landscape and the trends that we see continuing to evolve every day. We ensure we can rise to the challenge and meet the needs regardless of where we are currently.

Q Have you found trends within the collection preference and total white blood cells collected? What are some typical cell targets for collection? Are those targets usually met?

SB: The bulk of our collections are MNCs, and we are seeing most of the requests around 10 billion total cells, usually ranging from 8 to 12 billion. Most of the collections in our network (80% or so) are meeting those targets.

Q Why is standardization important to cell therapy collections?

SB: In terms of cell therapy collection and processing, standardization is helpful in making a process more efficient across the board, from setting up the protocol to collection. Then, the centers know exactly what to expect, and the manufacturer receives a quality product. Standardization can help fulfill the need for quality starting material and create steps to improve the quality. Standardization can also be a good step forward to get to commercialization.

AM: When you look at typical manufacturing processes of vaccines, biologics, and small molecules, the goal of the manufacturing team is to have control. You want control of your process and consistency in production, and a lot of that control and consistency come from where you start.

From a company standpoint, to ensure we have validated vendors, we have standards for incoming materials, so we expect reproducibility coming in. That really drives the control and reproducibility of our manufacturing process.

A level of variability naturally exists in cell and gene therapy, from donor variability to patient variability, all the way down to changing staff on-site or the hospital dynamic. When you receive products, you know there is going to be a certain amount of variability. Standardization is critically important to allow the supply chain to have a little bit more control and consistency, and limit variability as much as possible.

Look at your supply chain from a chemistry, manufacturing, and controls perspective and partner with your technical operations and clinical teams internally to figure out where can you partner with clinical sites to drive that standardization. This will ultimately help in your scalability and success.

Q What are some hurdles encountered in biotechnology in regard to apheresis, and how does leveraging BTMB considerations help to overcome them?

SB: From my perspective, a big hurdle is variability, as well as starting material quality. The most important thing is that a good material comes from the collection and processing and then arrives at the manufacturing. There are hurdles along the way, but that is the main goal.

From my perspective with the centers, making sure we cover all those considerations so that we come out with a good starting material is the biggest hurdle.

LA: The advantage that BTMB has is that when we utilize our collection network, we partner with centers that we work with day in and day out, so we truly understand how these centers are functioning.

We have touched on the numerous variabilities that are out there – staffing, training, logistics, processing, locations, natural disasters – anything that can impact a clinical trial. At BTMB, because we have that partnership with our networks, it feels like we are in tune with the centers throughout the entire process, and we are able to solve a lot of that variability.

When we select centers to participate in clinical trials, we examine the must-haves versus the nice-to-haves and consider which centers can accommodate this.

AM: When you are starting off in a new cell and gene therapy company, sometimes it can be challenging to find experienced employees. Funding issues can mean you have to keep your headcount smaller. However, you still have to deliver on the logistics and management of looking at clinical sites and apheresis collection centers. As Lacey said, BTMB really has a partnership with these centers. Plugging into an existing historical relationship with a lot of knowledge of how to move centers to a standardized area and how to partner with industry is a real advantage.

For a start-up biotech, having that capability in-house to be able to get your trials up as fast as possible, keeping your staff lean, and focusing on areas particular to your product is key. You can't always build out a 24/7 logistics monitoring group. You may not be able to hire someone who has an existing partnership with an apheresis center, or who knows how to interface and partner with them.

One of the greatest advantages BTMB is plugging into the machine that's already there, and being able to partner simultaneously with the team and the centers.

BIOGRAPHIES

Lacey Anderson

Senior Manager, Collection Network Management, Be The Match BioTherapies

Lacey and her teamwork to develop and manage our Collection Network for cell and gene therapies in clinical trials, interfacing between collection centers and cell and gene therapy developers. Lacey joined Be The Match BioTherapies in August 2019, bringing with her over 10 years of experience working in apheresis centers. She has held positions in center operations and quality management, as well as donor care supervision.

Sara Butler

Network Liaison, Be The Match BioTherapies

Sara serves as a liaison between Be The Match BioTherapies stakeholders, clients, and network centers. Sara also provides technical expertise and consultation to improve operational processes and Be The Match BioTherapies' product quality. Sara brings to Be The Match BioTherapies nearly a decade of cell therapy experience and knowledge of the industry.

Allison Montalvo

Program Manager, Oncology, Janssen (a division of J&J)

Allison has over 25 years of experience in biotech and pharmaceutical drug development (at Merck, Teva, Tmunity, and now Janssen). Before coming to Janssen, Allison was the Head of Project Management and Clinical Supplies at Tmunity. There, she led and developed integrated solutions for end-to-end supply chain management of CAR T trials.

AUTHORSHIP & CONFLICT OF INTEREST

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