How to Harmonize Best Supply Chain Practices for Apheresis?

Several Apheresis-related organizations are formulating standards for various aspects of the critical function of Apheresis in the evolving Cell and Gene Therapy. SMEs will explore how to simplify and improve the interface with Apheresis centers in areas of operations, systems, packaging, storage and logistics (particularly cold chain). Issues of compliance with regulatory standards will also be addressed. Listening to the Voice of the Customer and taking innovative, remedial steps will be the guiding principle for the exchange. Representatives from Standards Bodies (FACT and SCB) will present progress made and the challenges ahead.

Experts Address the Question at the BSMA Virtual Conference, August 5, 2021

PANELISTS

				
Dawn Henke, Senior Technical Program Manager, the **Standards Coordinating Body (SCB)**, a nonprofit organization which facilitates the development of standards for cell therapy, gene therapy and tissue engineering.	**Gary Hutchinson**, President of **Modality Solutions**, which is an engineering firm focused on the design and validation work on cold chain started 10 years ago in the biologics focused on monoclonal antibodies and CAR-T cells in recent years.	**Gregg Bodnar**, Client Engagement Head, **Be the Match BioTherapies**. The enterprise has been around for 30 plus years in stem cell transplants. Today it is engaged in cell and gene therapy as well.	**Olive Sturtevant**, Administrative Director of the cell manipulation core facility at **Dana-Farber Cancer Institute**, which serves as a CMO.	**Moderator: Peter Holman**, Vice President of Quality at **ArsenalBio.** Formerly, the Global Apheresis Integration Lead and Head of Apheresis Operations, **Novartis**.

PANEL DISCUSSION:

HOLMAN: ***What do you see as the biggest challenges to the field when it comes to the supply of the autologous cellular materials starting material for manufacturing?***

OLIVE STURTEVANT: Normally, I would talk about chain of custody and chain identity as one of the biggest concerns, especially with the autologous products, but I see a bigger issue with is getting the right cells collected from the patients. Not having the right information given to the apheresis centers about what the manufacturer wants and is not aware of the layer being pulled for the apheresis material and the type and volume of T-Cells. Being more specific about the cells to be collected for the biopharma companies may help with more success of manufacturing the product that you intend to manufacturer.

We follow the practices, as do all the accredited centers. I've been very vocal about accepting the ISBT 128 Labeling standard for both the outgoing material and the material coming back. You must maintain the identifiers that the clinical centers are going to use. So, the product can go out, get manufactured, come back and go to the patient, without needing to be relabeled. We generally spend a lot of time in contract negotiations and quality agreements to ensure that we get the information we need back on our products.

The other area that creates havoc is the variety of web portals and audits where different companies focus on different things. I think shipping has become standardized.

GREGG BODNAR: The biggest challenge is knowing the ongoing efforts to establish best practices and standards. I know, within my own organization, people don't know about the cryopreservation effort that's going on at PDA. Awareness will lead to adoption.

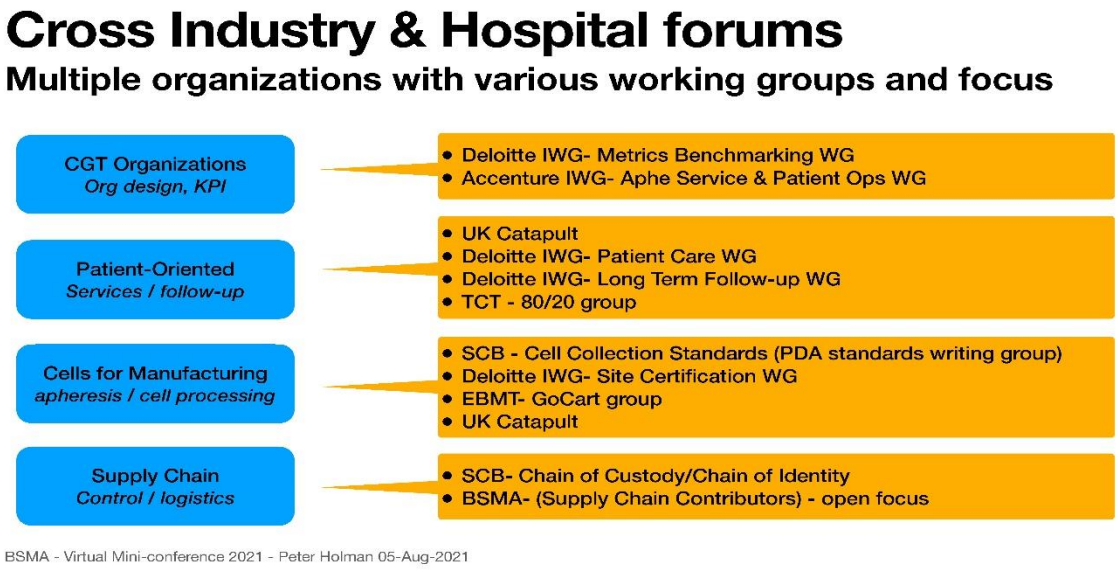
DAWN HENKE: Oftentimes, there's little differences in the cell collection procedures that could be standardized across the board because it becomes a huge burden on the centers, when they have multiple manufacturers, changing some of their procedures that are minor but often lead to errors. Multiple trainings and switching back and forth between S&OPs and those variations will become unnecessary. A standardized way of highlighting the inconsequential specific requirements would eliminate a huge barrier.

PETER HOLMAN: The CGT manufacturers must reduce the unnecessary variability imposed on hospitals. Furthermore, hospitals must also reduce the variability in their own processes. These harmonization and standardization concepts will simplify apheresis for manufacturers and hospitals alike. Some of these things which are filed may be in INDs, depending on the country where the apheresis centers may have filed with their Health Authority, what their processes are for collections and which bags they use and if a manufacturer wants a different bag, that may require the hospital to file a change as well. There are some challenges to organically harmonize and some for the standardization groups to formalize.

PETER HOLMAN: ***What improvements have you seen pertaining to variability of the requirements and the processes for starting cells for manufacturing?***

DAWN HENKE: I've seen a lot of improvement when it comes from the openness and willingness of companies to harmonize and work on standardizing. The challenge is their enactment.

PETER HOLMAN: I can chime in too. In 2019, I gave a talk at the ISCT International Conference in Melbourne about variability. In the last two years, an enormous amount of effort has gone into aligning and bringing these different groups together. There's a lot of membership of these groups and there's not a lot of redundancy. Here is the landscape.



OLIVE STURTEVANT: The clinical centers are dealing with different standards than the pharmaceutical companies are dealing with. I think for the academic centers for the collection centers, it continues to be a challenge.

GARY HUTCHINSON: At the intersection between the Clinical Standards and the GMP, companies are coming from GMP and biological manufacturing perspective and they want to see the apheresis collection as just an extension of the manufacturing process.

OLIVE STURTEVANT: Looking at the whole process, and really applying the changes that need to occur based on risk, helps because everybody to get on board.

DAWN HENKE: From a standards perspective, developing standards that are all encompassing and risk based, tend to be the best standards because they can be more flexible.

PETER HOLMAN: ***How does FACT's accreditation contribute to the harmonization of apheresis methods?***

GREGG BODNAR: It is very important for accreditation because we work with the Blood Center as well and EBB as well. We also perform quality audits. We've compared the requirements of GMP and GDP regulations. There is a lot of overlap between GMP and GDP and we have revised our audits to reduce the overhead and focus on quality versus the system.

OLIVE STURTEVANT: The institutions in the United States and Canada follow the FACT standards for collection but also around the world.

PETER HOLMAN: ***Are there some places where challenges are getting bigger, rather than making an improvement?***

DAWN HENKE: Data management has become a bigger challenge, more types of data being collected, more information and need for formatting consistency to enable tech transfer.

GREGG BODNAR: Companies are splitting organizations, for example, the vendor for network onboarding and supply chain logistics. I recommend let the CRO do both. Often in divided organizations, the responsibilities are unclear leading to finger pointing.

OLIVE STURTEVANT: We see confusion and overlap within one company where different groups are managing different clinical trials for basically the same product. Imagine how nurses carrying out the tasks are adversely affected!

PETER HOLMAN: ***We're looking to the future of CAR-T Cell therapy and potential outpatient procedures. US has a clear GDP. Certain hospitals have ISO 9000 at least, which is a step forward with quality management systems. Hospitals need to operate under 1271. I've seen a lot of centers that have their own labels that are essentially an ISBT label with slight differences. How can manufacturers facilitate accreditation bodies get into some of these centers, whether it's community centers or international centers?***

OLIVE STURTEVANT: I want to address with some of these products going to independent clinical centers, outside of a medical center or hospital. That's where a standardization becomes important because we must agree on what is that chain of identity to link the initial raw material back to the patient receiving that product in an unregulated facility.

GARY HUTCHINSON: The whole conversation of where does the GMP begin must be expanded. I'll just give an example. If the packaging that's used is currently sensitive on how it's used, preconditioning, for example, we've had a client who creates nuisance through nonconformances because if you can't get the pack out right, you will have temperature excursion on a fresh blood collection.

PETER HOLMAN: ***Will decisions around fresh versus frozen become a part of future apheresis standards or harmonization efforts?***

DAWN HENKE: I don't see any standards coming out to tell you to use cryo-preserved or fresh. I think different needs and different products will need different pathways.

GARY HUTCHINDSON: There definitely needs to be a standard on handling of fresh versus frozen. When the biologics and the monoclonal antibodies were first coming out, people were putting specific model numbers of packaging and very specific processes into their filing for their cold chain. The question for the industry was how should the package be qualified? And this is the best way to go about it which is very similar with the PDA did on thermal packaging for refrigerated products 20 plus years ago. You can't close Pandora's box at that point.

GREGG BODNAR: We have a client who has decided that that cryopreservation at the apheresis centers is not working for them. So, they are going to centralize their cryopreservation facility that that will give them better results on the product.

OLIVE STURTEVANT: We're working on the various groups to reach some consensus, and trying to harmonize, on the pharma side, as well as on the clinical side. But it is going to take a while.

GREGG BODNAR: We must minimize the specialized equipment and supplies as much as possible, because then it's a choice of either the manufacturer to supply it at the time of the therapy collection or therapy infusion. An apheresis center hospital finds it virtually impossible to inventory something for you. They don't have the space or the capability. So, one must work with generic suppliers as much as possible.

FINAL NOTE: The panel discussion has been an extraordinary learning for the entire industry.