Q&A SESSION WITH JOSEPH LANING

JOSEPH LANING, Director Cell Manufacturing Operations,
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Dr. Laning is currently the Director of Cell Manufacturing Operations at the Astellas Institute for Regenerative Medicine (AIRM). He received his BA degree in Biology from Boston University and his PhD in Immunology from Harvard University. He is a member of the International Society Cell Therapy and is the ISCT voting delegate to the USP. Dr. Laning has spent the past 24 years seeking to translate concepts into products in the fields of wound care, regenerative medicine, and stem cell therapies. He began his post-doctoral career at Organogenesis, Inc. where he developed and implemented pre-clinical investigations and subsequently managed all patient immunology safety testing leading to the approval of the PMA of ApligrafTM with the FDA. In 2002, he joined ViaCell, Inc. where he served as Director of Therapeutic Development and subsequently Senior Director of Analytical Biology. In these roles he oversaw strategic and operational scientific plans leading to successful approval of both IND and IDE filings and completion of the company's first clinical trial using allogeneic expanded cord blood stem cells. In 2010, he became Senior Director of the Massachusetts Stem Cell Bank and Registry and Research Associate Professor of Molecular Medicine at the University of Massachusetts Medical School. He served as Chief Technology Officer at Provia Laboratories leading strategic implementation of their cGMP cell and tissue banking operations. Current interests include developing and enhancing human iPS and ES manufacturing methods for delivery of drug substance and drug product for AIRM clinical programs and the scale up and automation of hPSC and derivative cultures to deliver commercial scale cell therapeutics.

What is your view on the overall outlook of Biomanufacturing in 2019?

Overall I'm quite optimistic about the outlook for Biomanufacturing for 2019. The interest in cell-based therapeutics has never been higher and between the increased investment in technology and infrastructure, the improved dialog with regulators about path and process, and the interest in regenerative medicine through industry and advocacy groups like ARM and PhRMA, the momentum continues.

What are the major restraints hindering progress in Regenerative Medicine Biomanufacturing?

Certainly, manufacturing capacity for both drug substance and drug product will be a challenge for both independent manufacturing entities and CMOs as more and more products move into trials and toward commercialization. Another factor that may hinder progress would be a lack of clear regulatory guidance on biomanufactured products of all types, biologics to cell therapies. Some of these guidance requirements or lack thereof may seem like esoteric topics but areas such as foreign matter contaminant limits (beyond USP or other guidances) or product/process comparability requirements at different stages of a product lifecycle are always lively topics at industry group meetings and conferences. One other significant potential restraint, which has been gaining some traction of late, is the availability and potential customization capability for single use culture ware and feeding systems. In particular, products that actually fit your process and development path. These systems are often geared narrowly toward scale-up of standard culture ware or jumping straight to bioreactors that do not fit your process. Scale-up can be a very time-consuming developmental trek and is related to patient dosing, supply chain requirements, and a host of other parameters. Ultimately, your process needs to deliver lot sizes that are enabling, whatever that size may be, and planning carefully can add downstream value.

What are the critical success factors for successful commercialisation?

I think primarily the importance of knowing your intended indication and understanding your product profile to the greatest extent possible should not be underestimated. The flipside of this is understanding your process and the ability to deliver on forecasted success is crucial. In understanding these pieces, you develop a product that will meet requirements. The strategy to move an ostensibly manual cell culture process forward and expect it to meet commercialization demands is likely unrealistic without automation. In addition interjecting automation technologies at the right stage and in the right place when it may be impossible to fully automate your process, brings value and ROI into sharp focus. Doing this, as you are moving through clinical trials adds to the enormity of the task.

The second piece is to consider is the thorough evaluation of your process materials and reagents early and often. This includes the manufacturers you procure from in order to head off shortages, regulatory uncertainties, and developmental improvements. Materials quality can be a downstream regulatory stop sign that you want to avoid. A clear path and some forethought can save time, expense, and pain in the future lifecycle of your product.

What are the biggest developments necessary for Cell Therapy Manufacturing for the future?

Many cellular therapeutics are multistage, complex processes that may take weeks or months to complete a single run, which may not be conducive to immediate full automation but could benefit from flexible, staged automation platforms for particularly labor intensive or tedious process steps. Robotics systems and automation vendors are beginning to fill some of these gaps but more can be done in this regard. Another area where progress might have a significant impact is in the field of testing technologies for product quality. Often times it seems that lot sizes for cellular products are often at odds with quality testing methods. This would pertain to product-specific testing for purity and potency for instance as well as the more well known quality parameters. Working towards testing technologies and regulatory requirements that maximize safety with an eye towards advances that minimize sampling burden seems like a win-win with the benefit being maximal information recovery the most frugal sampling profile possible.

In line with this last point, a more global perspective on regulatory requirements with EMA, PMDA, CFDA, and FDA working more closely to align requirements wherever possible will make product development and product lifecycle planning more cohesive and definitive. This could not be more true than for cellular therapeutics and regenerative medicine where seemingly subtle differences in regulatory guidances can lead to disruptive detours.