Developing a consensus on demonstrating monoclonality

"Biologic pharmaceuticals are inherently complex and variability in those molecules can have a tremendous impact on patient safety and efficacy," said Kyle Zingaro, Development Scientist at Alexion, and member of the Monoclonality point share of BioPhorum.

Manufacturing a consistent, homogenous product is vital. Regulators have been emphasizing the importance of demonstrating that a biologic is derived from a single-cell source, known as monoclonality, to ensure the safety and efficacy of a product. For decades, the old approach of limited serial dilutions of cells was widely accepted as the method of choice for demonstrating monoclonality. However, it has become increasingly recognized that newer, more advanced techniques produce more accurate results in a shorter time.

Whole-well single-cell imaging is rapidly gaining acceptance industry-wide and becoming the gold standard for demonstrating monoclonality. Other advances include techniques to deposit single cells, such as in-line imaging and microfluidic technology.

It is important that these new technologies are implemented and controlled in a consistent manner throughout the industry. The Monoclonality point share recognized the need to develop a consensus among the industry regarding the best practices and techniques to demonstrate monoclonality. It began its work by surveying its own members about what techniques each company was using to demonstrate monoclonality. This information was used to develop a consensus that imaging plate technology is a valid and acceptable technique to satisfy clonality.

During the past year, the point share has been busy creating a manuscript to promote its consensus. "The purpose of the manuscript is to bring together a large consortium of companies that produces biologics and advance a position to regulators and other companies regarding the best technology to demonstrate monoclonality," said David Shaw, Senior Scientist at Genentech. The manuscript describes how to establish an imaging-based workflow, the mechanisms to verify the performance of an imager, and case studies. The manuscript has been accepted for publication in the PDA Journal of Pharmaceutical Science and Technology in the summer.

The point share also presented its consensus on monoclonality at the Bioprocess International West Conference on March 20th, 2018 in San Francisco, California. Amie Lundquist, Senior Development Specialist II at Shire, presented on "Industry perspectives and case studies towards demonstration of monoclonality for biologics manufacture development."

Following completion of the manuscript and the presentation, the general consensus of the point share members is to move beyond monoclonality during the upcoming year. According to Shaw and Zingaro, the group intends to undergo a charter refresh and begin tackling issues regarding cell banks and other cell line development topics.

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PARTICIPATING IN A GROUP SUCH AS BIOPHORUM AND DISCUSSING ISSUES WITH OTHER COMPANIES IS A HUGE BENEFIT, AND ULTIMATELY ALLOWS US TO GET DRUGS TO PATIENTS IN A MORE TIMELY MANNER.

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Zingaro's experience in the monoclonality group has been extremely beneficial on both a professional and personal level. "Being involved in the Monoclonality point share has allowed me to gain expertise in the area of cell-line development and exposed me to a lot of ideas that my organization would not have had without being involved in BioPhorum. In the company, the accomplishments of the point share have facilitated a way for us to vet the imaging process and the approaches with regulatory bodies and scientists and provide confidence that the methods we are proposing are going to be accepted in the regulatory space," said Zingaro.

Shaw agrees that BioPhorum is an extremely beneficial organization. "Participating in a group such as BioPhorum and discussing issues with other companies is a huge benefit, and ultimately allows us to get drugs to patients in a more timely manner," said Shaw.