GMP Cytokines Optimization for Closed System T Cell Therapy Manufacturing

The Problem

Company focused on autologous T cell therapies targeting solid tumor cancers was progressing into clinical trials and needed to transition from research-grade to GMP-grade cytokines. Concurrently they wanted to improve their methods of cytokine supplementation to reduce cytokine waste, improve dose accuracy across lots, and reduce process risk by defining methods for closed-system cytokine addition. They were already using research-grade cytokines from Bio-Techne.

Company partnered with ScaleReady to simplify transition to GMP cytokines and address future waste reduction and closed-system cytokine addition.

Our Solution

As experts in recombinant protein manufacturing, we were able provide the following plan to address Company's immediate need to transition to Bio-Techne's GMP-grade cytokines and address future waste reduction and closed-system cytokine addition.

1. **Transition Plan for GMP cytokines** — For each GMP cytokine, ScaleReady provided Company a certificate of analysis, stability data, and bioactivity documentation for specification comparison against research-grade cytokines. Company confirmed that the GMP-grade cytokines of interest use the same clone and manufacturing process as the research-grade cytokines. Next, three lots of each GMP cytokine were provided to the company for performance equivalency and lot-to-lot consistency testing.
2. **Cytokine Use and Waste Reduction Plan** — Company was ordering cytokines in vialled amounts larger than required for a single process dose. This resulted in discarding of unused reconstituted cytokine. We provided options for reducing waste, including offering custom activity (IU) per vial filling and off-the shelf cytokines in smaller vialed amounts.
3. **Closed-system Plan for GMP Cytokines** — Looking to commercial manufacturing, this company was interested in reducing process risk by implementing closed-system addition of GMP cytokines. We provided some prototype closed-system cytokines in bags for Company to evaluate for ease-of-use and performance equivalency. We are open to partnering with companies to identify the best solution for closed-system cytokine addition for cell therapy manufacturing.

The Outcome

- **Converted from Research-grade to GMP Cytokines** — Company generated data showing comparable bioactivity of GMP and research-grade cytokines. Additional data showed consistent lot-to-lot performance of GMP cytokines in their process. Together, these data allowed them to document and justify the transition to GMP.
- **Enacted Plan to Reduce Cytokine Waste** — Group identified that 2 of 3 GMP cytokines were available off-the-shelf at smaller sizes that met their minimum activity per vial requirements. Switching to smaller vialled amounts helped reduce cytokine waste. For the remaining cytokine, Company is pursuing custom vialing to deliver process-fit activity per vial, thus eliminating waste for that GMP cytokine.
- **Exploring Option for Closing Cytokine Supplementation** — Company is open to working with ScaleReady to explore options for future closed-system cytokine addition.

	GMP Cytokines Off-the-Shelf Vial			GMP Cytokines Custom fill	Closed-system GMP Cytokines
	Aliquot EXACT amount for process	Measure EXACT amount every time	Use the entire vial contents	Exact amount for process	Exact amount for process
Clean Room Time					
Adaptable to Automation					
Risk (handling/error)					
Operator Time					
Waste					
Favorable for Cell Expansion					

Figure 1. Commercial options for GMP cytokines and their impact on time, risk, waste, and ability to fit into closed-system cell manufacturing platforms.

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