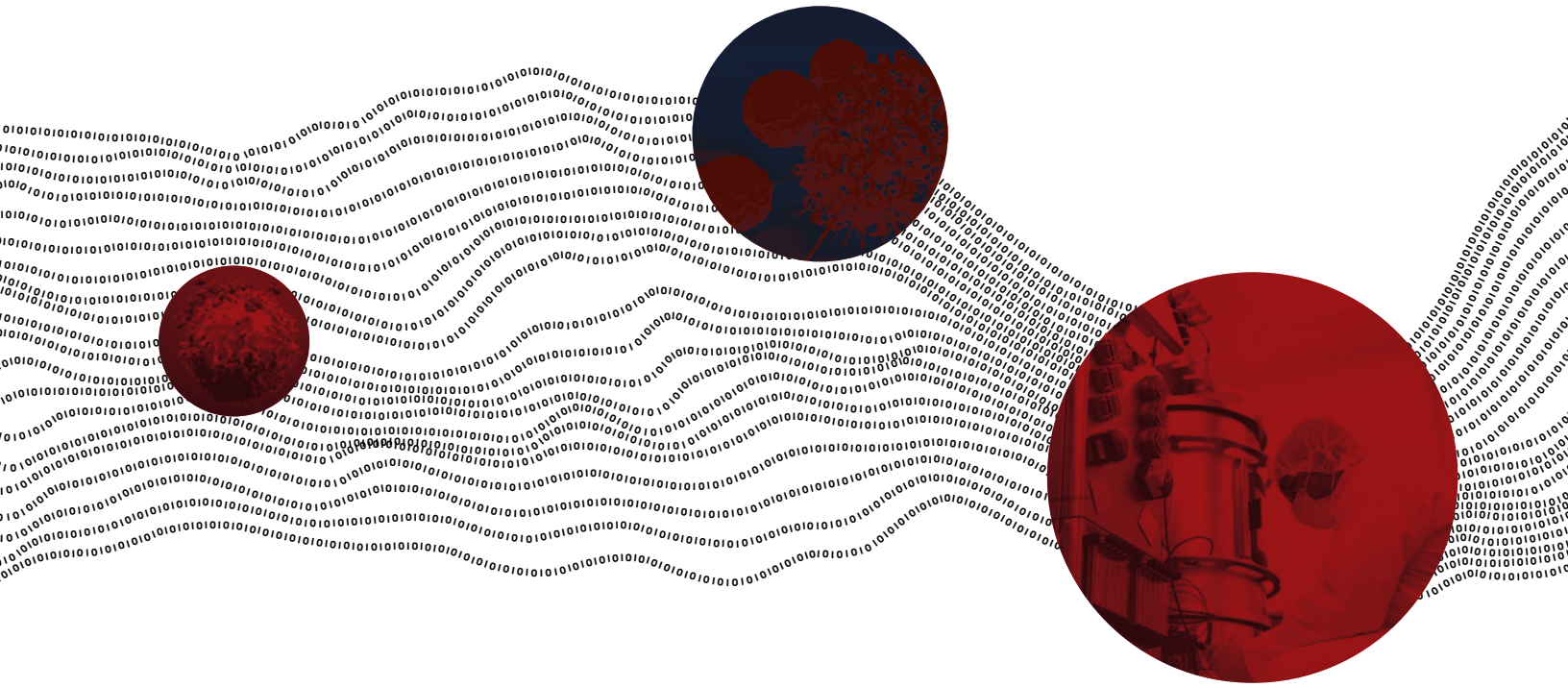
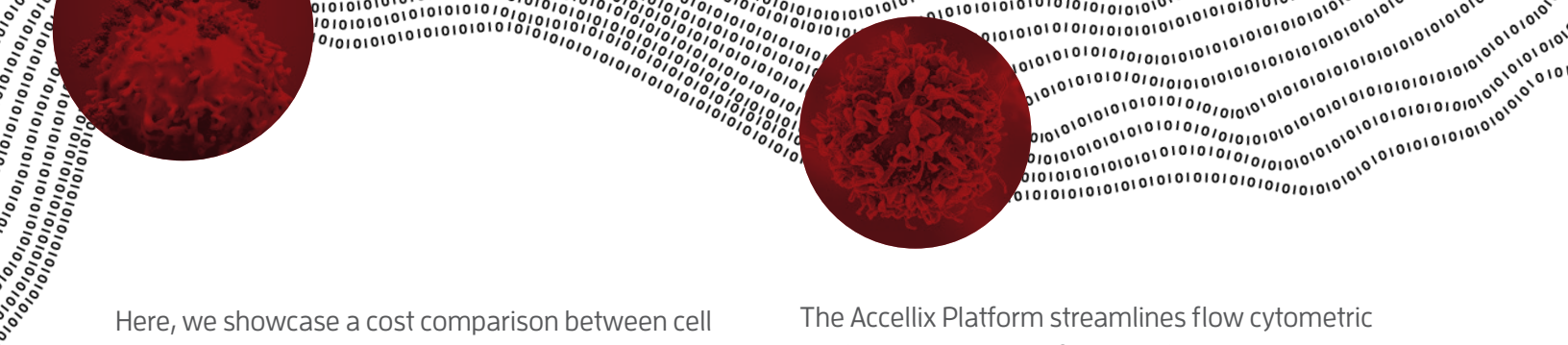
COST ANALYSIS

COMPARING CELL THERAPY MANUFACTURING QC COSTS OF TRADITIONAL FLOW CYTOMETRY VERSUS THE ACCELLIX PLATFORM



Accellix



Here, we showcase a cost comparison between cell therapy flow cytometry QC on the Accellix Automated Cell Phenotyping Platform versus a traditional flow cytometer. By automating a complex and laborious process, and by bringing flow cytometry directly into the GMP manufacturing suite, the Accellix Platform reduces the costs of labor, reagents, QC lab space and instrument by 50-300% (Figure 4), enabling cell therapy manufacturers to scale QC to a growing patient population.

Flow cytometry, an indispensable tool in many areas of biology, serves as the gold standard for cell analysis in cell therapy manufacturing. Using a single platform, cell therapy manufacturers can measure a variety of parameters, including cell viability, potency, genetic engineering efficiency, and phenotype. Despite its utility in cell therapy research and development, traditional flow cytometry is not easily transferable into the GMP manufacturing environment due to the complexity and variability associated with individual operator handling, reagents, instrument setup and maintenance, sample preparation, data acquisition, and analysis. This complexity is also associated with a high cost, which is largely driven by the need for highly trained personnel to execute many manual steps. In addition, flow cytometers tend to be very expensive to purchase, costly to maintain, and require a centralized flow cytometry Quality Control (QC) lab space to operate in.

As more cell therapies are approved and become first-line therapies for some indications, the increased patient load will make it nearly impossible to manufacture and QC sufficient samples using the processes in operation today. Increased cell therapy manufacturing will require recruiting, training, and retaining a larger number of highly skilled and well compensated flow cytometry technicians (Ham et al). Considering that a talent gap already exists in the cell therapy manufacturing space, there aren't enough qualified personnel to execute QC workflows, and the associated costs will remain prohibitively high for patients and insurers (Piller, M).

The Accellix Platform streamlines flow cytometric analysis in GMP manufacturing by automating sample preparation and data analysis; the most manual, variable, and laborious workflow steps. The Accellix Instrument can be operated directly in the GMP manufacturing suite, eliminating the need for a centralized flow cytometry QC lab and requiring only one hour of training. Less-skilled and lower-paid technicians can operate the platform with fewer operating costs to purchase and maintain. Here we highlight a cost analysis comparing a typical flow cytometry QC workflow to the Accellix workflow, revealing the cost savings associated with adopting the Accellix Platform in clinical scale cell therapy manufacturing.

CONSIDERATIONS

Phenotyping Steps: For this analysis, we used a representative CAR-T cell manufacturing workflow with five phenotyping steps during the process (Figure 1). At several phenotyping steps, a single antibody panel is employed on the traditional cytometer, while the panels are separated into two kits on the Accellix Platform (Figure 2). In practice, all of the cell surface markers may not need to be analyzed in every workflow. For ease in calculating costs, we assumed that all five phenotypic analysis per patient would occur on a single day, though, in reality, they can be spread across several weeks.

1. Starting Material: The starting material (e.g., apheresis) is analyzed to determine the viability and frequency of CD4+ and CD8+ T cell populations, as well as non-T cells like CD19+ B cells and CD14+ monocytes.

2. Post-selection: We assume that purified T cells are the desired input material for this workflow. Therefore, we include a phenotyping step after cell selection (e.g., via ficoll separation or magnetic beads) to assess the purity of the post-selection cells.

3. Post-modification: Several days after cells are genetically modified (e.g., via lentiviral transduction), we assume that cells are analyzed to assess the efficiency of modification using an antibody panel containing an anti-CAR antibody.

4. Expansion: During the expansion phase, we assume that cells are analyzed to ensure the cell modification remains stable and that the relative proportion of T cell subsets is maintained.

5. Formulation/Release: Prior to final cell product formulation and release to patients, we assume that cells need to be analyzed to determine viability, proportions of CAR+ T cell subsets, and the presence of contaminating cell populations.

	Starting Material	Post-Selection	Post-Modification	Expansion	Formulation/ Release
Traditional Flow Cytometer	1 TBMNK panel w/o CAR	1 TBMNK panel w/o CAR	1 TBMNK panel w/ CAR	1 TBMNK panel w/ CAR	1 TBMNK panel w/ CAR
Accellix	1 T Cell Assay 1 Lymphocyte Assay	1 T Cell Assay	1 CAR Assay	1 CAR Assay	1 Lymphocyte Assay 1 CAR Assay

FIGURE 1. PHENOTYPING STEPS DURING REPRESENTATIVE CAR-T CELL MANUFACTURING PROCESS.

TRADITIONAL FLOW CYTOMETER	ACCELLIX		
TBMNK	**T CELL SUBSET ASSAY**	**LYMPHOCYTE SUBSET ASSAY**	**CAR CUSTOM ASSAY (REPRESENTATIVE)**
CD45	CD45	CD45	CD45
CD3	CD3	CD3	CD3
CD4	CD4	CD14	CD4
CD8	CD8	CD19	CD8
CD14	Viability	CD16	anti-CAR
CD19		CD56	Viability
CD56		Viability	
Viability			
anti-CAR (as needed)			

FIGURE 2. ANTIBODY PANELS USED ON A TRADITIONAL FLOW CYTOMETER VERSUS THE ACCELLIX PLATFORM.

Labor Costs: Traditional flow cytometry requires highly trained, specialized staff who must be compensated accordingly. Thus, we estimated a $75/hour salary for these employees. In contrast, the Accellix Platform can be operated by anyone within one hour of training, as most of the workflow is automated and does not require skilled manual labor (Figure 3). Furthermore, Accellix's algorithm-based automated data analysis also eliminates the need for these operators to perform complex, time-consuming, and subjective data analysis. Therefore, we estimated a $40/hour salary for these employees.

	TRADITIONAL FLOW CYTOMETRY WORKFLOW (MINUTES)	ACCELLIX WORKFLOW (MINUTES)
Thaw + Prepare Cells	60	21
Assay Execution	90	26
Instrument Setup	15	0
Data Acquisition	30	0
Data Analysis	90	0
Total FTE Hands-On Time	285	47

FIGURE 3. HANDS-ON LABOR BREAKDOWN TO ANALYZE SAMPLES FROM ONE PATIENT ON TRADITIONAL FLOW CYTOMETER VERSUS ACCELLIX PLATFORM.

Reagents: Each Accellix Assay contains dried, unitized and room temperature stable reagents that are ready for use immediately. In contrast, antibody labeling for traditional flow cytometry experiments typically requires aliquoting small volumes of multiple reagents to generate an antibody cocktail and dependence on a cold chain. The remaining reagent leftover in the antibody tubes may be used in subsequent experiments, though some cell therapy manufacturers opt to use the entirety of each antibody tube for processing a single patient. Thus, we include a range of reagent costs depending on whether the fluorescent antibodies are sub-aliquoted or not.

QC Flow Cytometry Space: Because of its small, fan-less design, the Accellix Instrument may be operated directly in the GMP manufacturing suite, obviating the need for a centralized, flow cytometry QC space. Therefore, we removed the cost for this space in the Accellix cost calculation.

Instrument Costs: We assume that a facility will require at least two flow cytometers—one to operate and one for backup, though we included three Accellix Instruments to increase throughput. We estimated that a traditional cytometer with a service contract costs $365,000, while an Accellix Instrument with a service contract costs $82,000 and amortized this cost over seven years.

COST ANALYSIS

	TRADITIONAL FLOW CYTOMETRY WORKFLOW	ACCELLIX WORKFLOW
Labor Cost per patient*	$356	$31
Staining Reagents per patient	$451-$2200	$850
QC Flow Cytometry Space per day	$542	$0
Instrument Cost per day	$435	$98
Total Cost	$1784-$3533	$979

FIGURE 4. COST BREAKDOWN TO ANALYZE SAMPLES FROM ONE PATIENT ON A TRADITIONAL FLOW CYTOMETER VERSUS THE ACCELLIX PLATFORM.

*Labor cost only considers hourly wages and does not account for additional costs associated with a fully burdened employee.

Based on the assumptions described earlier, we calculated the cost required to phenotype five samples per patient in a GMP clinical manufacturing setting utilizing a traditional flow cytometer in a centralized flow cytometry QC lab versus the Accellix Platform within the manufacturing suite. Due to the highly manual nature of the traditional flow cytometry workflow and the qualifications required from this employee, we estimated $356 in labor costs in this process, versus only $31 in the automated Accellix workflow.

We calculated the cost in staining reagents required to process five samples in triplicate for traditional flow cytometry assuming that either antibodies are sub-aliquoted and stock vials are used for multiple patients, or a single tube of antibody is consumed per patient. This yielded a range of $451–$2200 per patient in staining reagents for the traditional flow cytometry workflow, versus $850 in the cartridge-based Accellix workflow.

We estimated that a 2,000 square foot centralized flow cytometry QC lab is required to process patient samples on a traditional flow cytometer and determined that this space costs $542 per day. Given that the Accellix Instrument can operate within a clean room manufacturing suite, we assigned $0 to this cost in the Accellix workflow. In comparing the instrument cost, we estimated that purchasing and maintaining two traditional cytometers costs $435 per day, while purchasing and maintaining three Accellix Instruments costs $146 per day.

In total, we estimate that it costs between $1784 and $3533 to phenotype five samples for one patient on a traditional flow cytometer. In contrast, the automation and simplicity of the Accellix workflow decreases the cost by at least 50% to $979, potentially even decreasing the cost by more than three-fold depending on the reagent costs.

As cell therapies become accessible to more patients, manufacturers will process greater numbers of samples in parallel. To evaluate the costs of scaling manufacturing to greater numbers of patients, we calculated the cost to perform flow cytometry on 1, 5,10, and 40 patients, continuing to assume five phenotyping samples per patient (Figure 5). In this calculation, we used the higher reagent cost associated with clinical manufacturing and assumed that two traditional cytometers and four Accellix Instruments will be employed to meet the higher throughput needs. As expected, costs increased with increased patient numbers for both platforms, but interestingly, costs increased less dramatically when the Accellix Platform is used. By calculating a slope for each dataset, we found that the costs increased at a rate of $3607 per patient using the traditional flow cytometer, while they increased at a rate of $1092 per patient using Accellix .

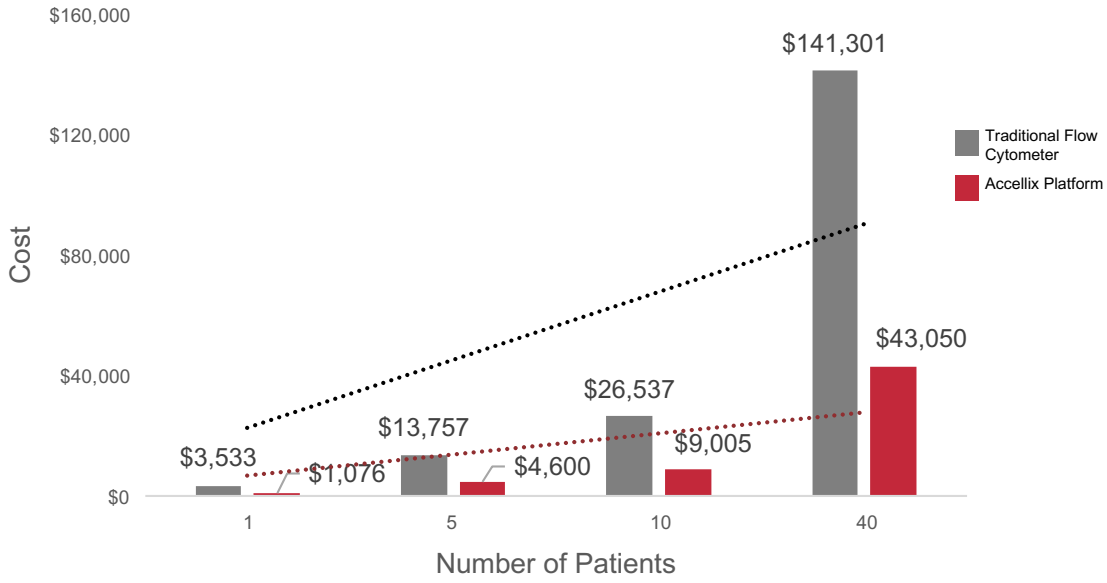


FIGURE 5. COST TO SCALE QC FLOW CYTOMETRY IN A GMP ENVIRONMENT. Bar graph shows cost to perform flow cytometry on samples from 1, 5, 10, and 40 patients on a traditional flow cytometer (gray) and the Accellix Platform (red). Dotted lines represent linear regression trendlines associated with each dataset.

CONCLUSION

Reducing the cost to manufacture cell therapies is critically important for broadening the accessibility of these potentially curative therapies to larger patient populations. QC of the cell products represents a significant cost driver and traditional flow cytometry is not scalable in its current form. The Accellix Platform reduces these costs by simplifying and automating the most manual steps in the flow cytometry process. By bringing flow cytometric analysis directly into the manufacturing suite where it can be performed by minimally trained operators, the platform increases reproducibility, lowers error rates, and reduces costs by up to three-fold per patient, enabling cell therapy developers to scale their manufacturing to meet the demands of the future.

REFERENCES

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Matthew Pillar. https://www.bioprocessonline.com/doc/taking-on-the-talent-crunch-in-biopharma-cell-gene-manufacturing-0001

To learn more about the Accellix Platform, email us at **info@accellix.com**

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