Cost-Effective Scaling of Cell Therapies:

Whitepaper | Vertical-Wheel® Bioreactors vs Traditional Systems

Cell-based therapies demonstrate remarkable potential as next-generation treatments for many conditions. However, the promise of cell therapy hinges on solving a critical challenge: how to generate **large numbers of high-quality cells** from limited donor material at a **commercially viable cost.**

During cell therapy, a single therapeutic dose often requires on the order of 10^8–10^9 cells.
A comprehensive clinical series may require multiple doses per patient. Conventional methods of cell culture, such as planar culture flasks and stirred-tank bioreactors, are both logistically impractical and prohibitively expensive for growing cells at these numbers. These constraints are pronounced when working with sensitive cell lines, such as stem cells, which require homogeneous environments and gentle handling to maintain their clinical quality.

PBS Biotech presents a novel solution:
the Vertical-Wheel® bioreactor. This technology combines uniform low-shear mixing, single-use closed vessels, and scalable geometry—from 0.1 L to 80 L—to offer a promising option for cost-effective, GMP-compliant cell production.

This white paper presents a detailed cost analysis, comparing Vertical-Wheel bioreactors to traditional and emerging cell culture methods. Discover how Vertical-Wheel technology enables the delivery of **quality at scale**, making commercial cell therapy manufacturing both technically feasible and economically sustainable.

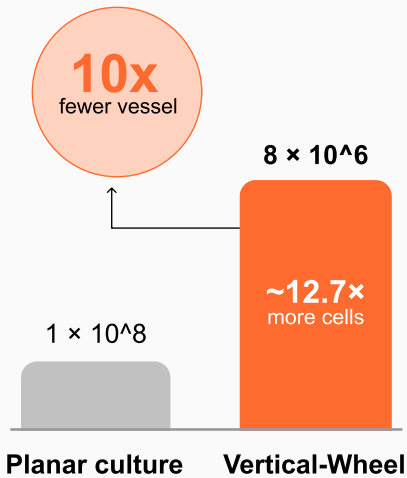
Expansion Efficiency

An essential metric for any cell culture platform is the efficiency with which starter cells can be expanded into high-quality therapeutic doses. Traditional planar culture requires serial stepwise “scale-outs” that are both slow and labor-intensive, with a risk of flask failure at each passage. Stirred-tank bioreactors offer larger batches, but at shear forces that can damage delicate cell lines, such as induced pluripotent stem cells (iPSCs) and mesenchymal stem cells (MSCs).

The Vertical-Wheel bioreactor allows larger expansions in a single batch, dramatically reducing the number of passages without compromising cell integrity. In direct comparisons with planar culture systems, iPSCs grown on equivalent surface areas in Vertical-Wheel systems demonstrate:

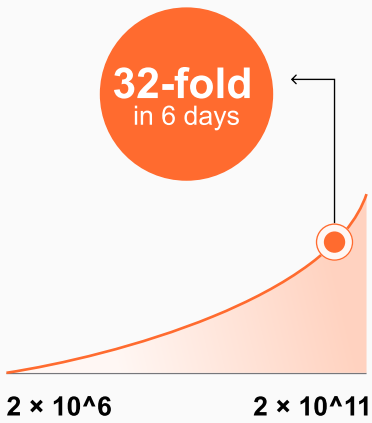
Higher Yields per Batch:

Vertical-Wheel systems produce **~12.7×** more iPSCs than planar culture on equivalent surface area (e.g., 1 × 10^8 vs 8 × 10^6 cells) in one run, reducing vessel count by an order of magnitude.[1]



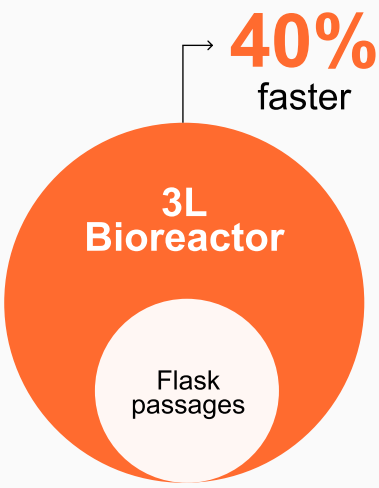
Rapid Fold-expansion & Higher Density:

Human iPSCs expanded 32-fold in 6 days with a single 50% media exchange, reaching clinical scale over four passages from 2 × 10^6 to >2 × 10^11 cells at nearly double the density achieved through multiple planar passages.[2]



Fewer Scale-up Steps:

One 3 L bioreactor run can replace dozens of flask passages, reducing media use by approximately 50% and time by approximately 40% compared to planar methods.[3]



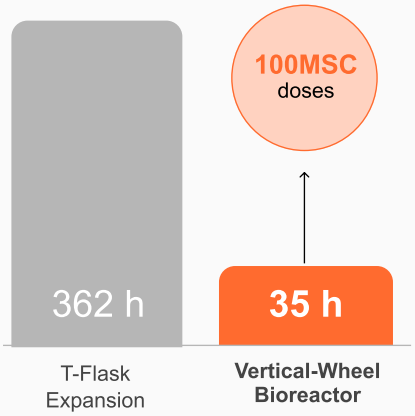
These results are possible thanks to the gentle hydrodynamics of the Vertical-Wheel design, which delivers superior mixing and oxygenation that support rapid cell growth without sacrificing uniform growth conditions. Vertical-Wheel systems enable the rapid expansion of limited donor cells into therapeutic doses without compromising cell quality or risking phenotypic integrity.

Streamlined Staffing

A major cost driver in cell therapy manufacturing is laboratory labor. Technicians must follow complex schedules to seed, feed, monitor, and harvest hundreds of individual vessels. Each manual process consumes skilled operator time and introduces risk for contamination.

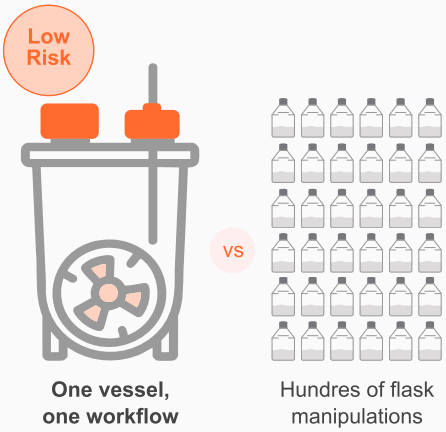
Enclosed single-use systems, such as the Vertical-Wheel bioreactor, reduce steps and enable automation to ease labor demands. In direct comparisons, these expansions deliver:

Up to 90% Labor Savings



Producing 100 MSC doses (10^6-cells) via manual T-flask expansion required ~362 h of labor versus ~35 h for an automated single-use bioreactor.[4]

Reduce Interventions



One vessel, one workflow—versus hundreds of flask manipulations—minimizes errors, contamination risk, and quality control (QC) burden.

Operator Efficiency

Fewer batches in a single bioreactor means fewer vessels to handle, monitor, and QC test, freeing skilled staff for higher-value tasks.[5]

Vertical-Wheel bioreactors enable a **lean staffing model** for cell expansion. By automating mixing and environmental control, and by consolidating production into far fewer vessels, organizations can enjoy a **10-fold reduction in labor costs** for comparable cell production.

Lean Facilities

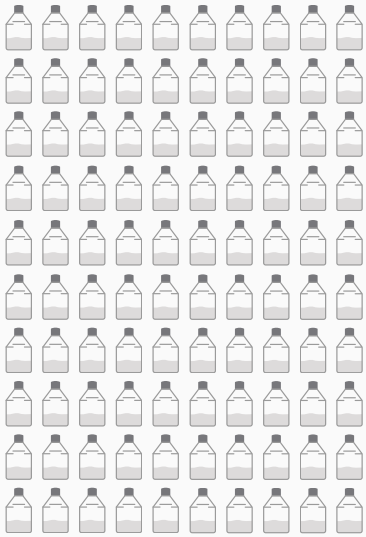
Traditionally, cell culture requires highly specialized facilities with infrastructure for clean rooms and incubators, as well as the capacity to scale. Vertical-Wheel technology enables lean facilities by delivering the same cell counts in a smaller footprint, utilizing single-use vessels that reduce infrastructure demands.

Vertical-Wheel

A 3 L unit (2×3 ft footprint) can replace ~100 T-175 flasks; **dozens** of reactors fit easily in a **500 ft²** suite. Single-use sterile vessels in an enclosed system with integrated environmental controls need rooms with only basic HVAC support.

1 x 3 L unit

=



~100 T-175 flasks

Planar Culture

Thousands of T-flasks require multiple CO_2 incubators and biosafety cabinets, which are housed in ISO 7 cleanrooms. **10,000 ft²** or more may be required for high-dose production.

Stirred-Tank Bioreactor

To reuse large-scale bioreactors, massive autoclaves, clean-in-place (CIP) or steam-in-place (SIP) infrastructure is necessary.

With an automated bioreactor process, **facility costs are cut by more than half**.[4] Therapeutic dose cell counts can be achieved in smaller spaces, while the closed, single-use nature of Vertical-Wheel bioreactors delivers GMP compliance without complex facilities infrastructure.

Consistent Outputs

Consistency and reproducibility of the cell product are paramount in cell therapy – patients, clinicians, and regulators expect that each batch of cells will have the same quality attributes, regardless of the scale at which they were produced.

A common problem with high volume expansions is batch variability. When you culture cells in 100 separate flasks, slight differences in conditions or handling can lead to heterogeneity in the final cell population.

In stirred-tank systems, the move from small flasks to large bioreactors is often challenging. The unique construction of Vertical-Wheel systems creates predictable, uniform environments regardless of scale - the conditions in a mini 0.1 L bioreactor can be easily replicated in bioreactors as large as 80 L.

Uniform Hydrodynamics

Vertical impeller design eliminates stirring dead zones to ensure all cells experience similar conditions, with a geometry that delivers linear scale-up and consistent cell growth from 0.1 L to 80 L. Vertical-Wheel bioreactors operate at **25% the peak shear of stirred-tank systems**, supporting the high quality growth of sensitive cell lines like hiPSCs[4] and MSCs[6].

Batch Reproducibility

The ability to grow larger batches in a single vessel naturally eliminates batch-to-batch variability at high cell numbers. MSCs expanded in a single bioreactor versus multiple T-175 flasks exhibit **more uniform phenotypes and double at a more consistent rate**. Consistent phenotypes and growth rates are repeatable, with **less than 5% variance between batches.**[5]

Scalable Consistency

Vertical-Wheel systems offer one of the only truly linear scale-up processes for cell culture. Thanks to homogenous mixing and gas transfer, iPSC and MSC processes developed at bench scale translate directly to pilot and manufacturing scales without the need for process re-engineering at each step up.[4]

The Vertical-Wheel system provides a **stable, uniform culture environment** that promotes reproducibility across every batch, every time.

Therapeutic Quality

Ultimately, the true test of any cell expansion technology is the quality of the cells produced – their biological functionality, safety, and genetic stability. A cost-effective process is meaningless if the expanded cells lose their therapeutic potency.

Cells grown in PBS Biotech's Vertical-Wheel bioreactors reach the large quantities needed while retaining the critical quality attributes required for clinical use, which are equivalent to or superior to those of cells grown in conventional systems.

Genetic Integrity	Vertical-Wheel bioreactors have demonstrated the ability to facilitate massive expansion numbers while maintaining a cell line's fundamental properties. iPSCs expanded approximately 100,000-fold over four passages retain a normal karyotype, high expression of pluripotency markers, and full differentiation capability.[2]
Consistent Phenotype & Potency	MSCs expanded in Vertical-Wheel reactors maintain defining markers (CD73, CD90, CD105) and exhibit tri-lineage differentiation and immunosuppression meeting or exceeding that of flask-grown cells.[5] These cells demonstrate therapeutic potency as well, inhibiting inflammatory cytokine release as well or better than flask expanded cells.[4]
High Viablity & Safety	The build of Vertical-Wheel systems supports cell health and consumer safety. Low-shear mixing maintains >90% viability at harvest, with low stress markers. Closed, single-use runs dramatically lower contamination risk and cell variability, delivering a safer product for patients.[4]

Vertical-Wheel bioreactors enable **cost-effective large-scale cell production without compromising quality.** Both stem cells and differentiated cells grown in these systems have been shown to retain their essential characteristics: normal genetics, correct phenotype, and therapeutic function. Whether it's iPSCs maintaining pluripotency after massive expansion[2] or MSCs maintaining immunosuppressive efficacy[4], the evidence suggests that Vertical-Wheel culture is fully compatible with the demands of cell therapy products.

Side-by-Side Comparisons

When comparing traditional and modern culture systems, Vertical-Wheel bioreactors emerge as a cost-effective system to deliver quality at scale.

Metric	Planar (Flasks/Stacks)	Stirred-Tank Bioreactor	Vertical-Wheel® Bioreactor
Yield per Vessel	**Low** – 10^7–10^8 cells per vessel (e.g. ~1×10^8 per 10-layer stack)	**High** – 10^9+ cells per vessel (large volume); requires microcarriers for adherent cells	**Very High** – 10^8–10^9 cells per vessel; scales to >10^11 in large single-use units
Time to Reach 1 M Cells (from a small seeding)	**Slow** – requires multiple sequential passages over 2 weeks	**Fast** – can often achieve the target in a single batch (5–7 days)	**Fast** – achieved in a single expansion (6 days); minimal pre-expansion needed due to low seeding density capability
Labor hours per batch (100 M cells)	**High** – extensive manual handling due to many small vessels; **~3–4 hours**	**Moderate** – some automation, but setup/harvest of large reactor and microcarriers needed; **~1–2 hours**	**Low** – highly automated, single unit process with minimal handling; **~0.3–0.5 hours**
Facility Footprint	**Large** – requires many incubators and biosafety cabinets; high cleanroom space per batch	**Medium-Large** – large floor-standing bioreactors; may need CIP/SIP	**Small** – compact; minimal cleanroom requirements
Contamination Risk	**High** – many open handling steps across vessels	**Low** – usually a closed system; CIP/SIP needed if steel (risk if cleaning fails)	**Low** – closed single-use vessel; fewest entry points for contaminants

Assumptions: Planar based on multiple T-175 flasks or 10-layer factories; stirred-tank ~50 L single-use bioreactor with microcarriers; Vertical-Wheel based on 3 L PBS Biotech system. Costs are rough estimates from published studies and assume all include GMP QC and similar media. Actual values will vary by process. Vertical-Wheel consistently shows the lowest cost per cell due to labor and material efficiencies.[3,4]

Quality at Scale

PBS Biotech's Vertical-Wheel bioreactors deliver higher yields, faster expansion, lean staffing, compact facilities, consistent outputs, and therapeutic-grade cells at the lowest cost per cell—a compelling solution for the cost-effective and scalable manufacturing of cell-based therapies.

Learn more about how Vertical-Wheel bioreactor technology can transform your cell therapy manufacturing process:

Contact PBS Biotech | Learn More

References

1. Verhoeff, K., *et al.* (2025). Scalable bioreactor-based suspension approach to generate stem cell–derived islets from healthy donor-derived iPSCs. *Transplantation,* 109(1), e22–e35.
2. Borys, B.S. *et al.* (2020). Optimized serial expansion of human induced pluripotent stem cells to clinically relevant quantities in vertical-wheel bioreactors. *Stem Cells Translational Medicine,* 9(9), 1036-1052.
3. Haskell, A., *et al.* (2024). Scalable manufacture of therapeutic mesenchymal stromal cell products on customizable microcarriers in vertical wheel bioreactors that improve direct visualization, product harvest, and cost. *Cytotherapy,* 26(4), 372–382.
4. Nogueira, D.E.S. *et al.* (2021). Single-use bioreactors for human pluripotent and adult stem cells: Towards regenerative medicine applications. *Bioengineering,* 8(3), 68.
5. de Sousa Pinto, D. *et al.* (2019). Scalable manufacturing of human MSCs in the vertical-wheel bioreactor system: an experimental and economic approach. *Biotechnology Journal,* 14(12), e1800716.
6. Marklein, R.A. & Warnock, J.N. (2021). Biomanufacturing of Mesenchymal Stem Cells for Therapeutic Applications. In *Cell Engineering* (pp. 271-297). Springer.