Corning® Ascent®
Fixed Bed Reactor System

Scaling from Process Development to Production with a High Density Adherent Cell Growth Platform

CORNING

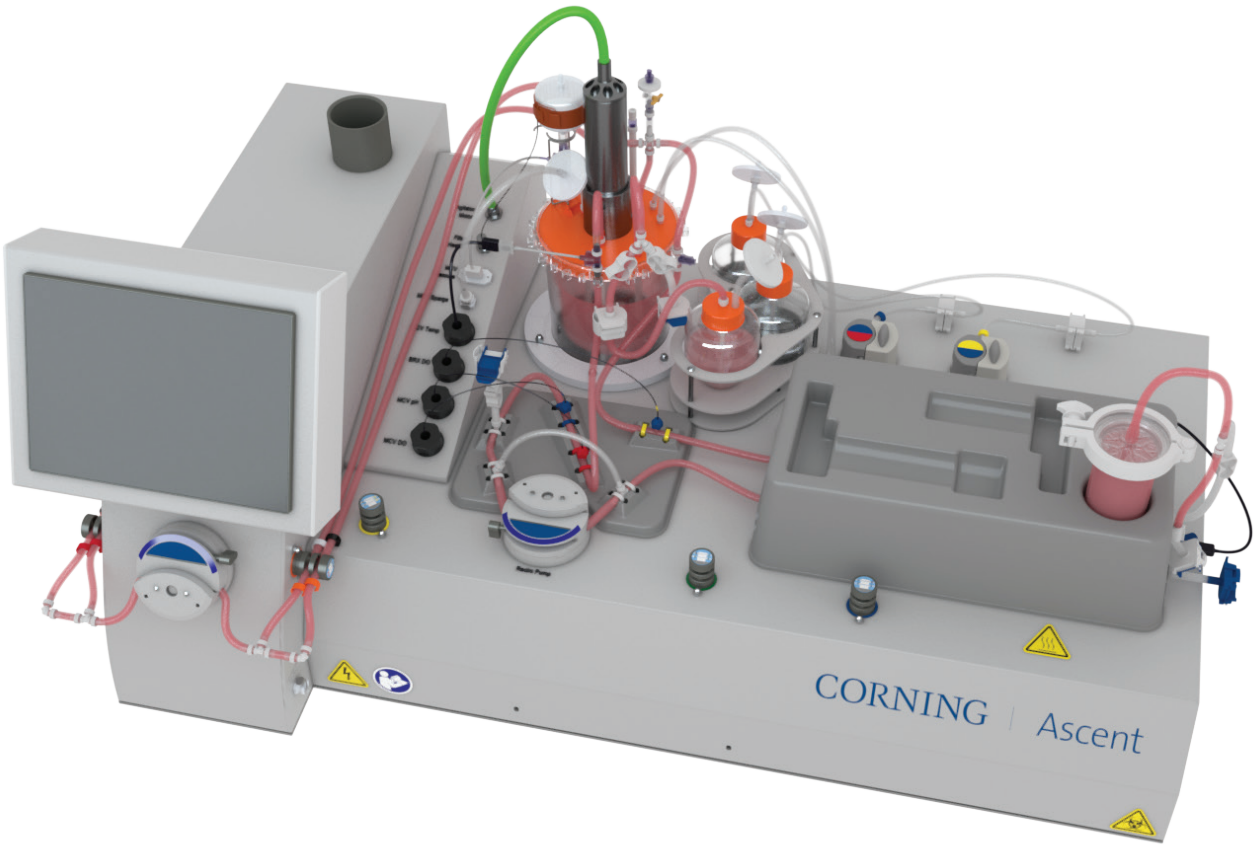
A major challenge in manufacturing adherent cells for advanced therapies is producing the large quantities of cells needed in a cost-effective manner. Corning has developed a novel fixed bed bioreactor platform that is designed to deliver significant surface area intensification and high-yield bioproduction capability.

The Corning Ascent FBR System is designed to enable process development and production scale cell culture capacities for cell and gene therapy workflows with high yields and viable cell harvest capability that may result in substantial cost savings when compared to existing commercial FBR systems.

Advances in cell and gene therapy, biotherapeutics, and more, require technological innovation

Recent advances in biotherapeutics and cell and gene therapy may hold unprecedented promise for difficult-to-treat health conditions. From oncology to diabetes to rare diseases, innovative and rapidly evolving technologies continue to pave the way for potential treatment options once thought impossible.

For example, in gene therapy, recombinant adeno-associated (AAV) and lentiviral vectors (LVV) have emerged as leading gene delivery tools for *in vivo* and *ex vivo* gene therapies, respectively. However, most existing manufacturing technologies for these modalities are either labor-intensive, costly and slow, not truly scalable, or some combination thereof. Now more than ever, the industry needs scalable, cost-efficient manufacturing of cells and cell products such as viral vectors.



An improved system for cell and gene therapy workflows

To address the need for a more efficient solution, we developed the Corning® Ascent® FBR System, designed to combine the benefits of adherent bioproduction platforms with the scale and automation of suspension manufacturing systems.

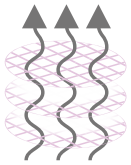
The innovative bioreactor design in the Ascent FBR is designed to enable uniform media flow to enhance cell health and drive uniform high-density cell growth. It has demonstrated greater than 90% transfection efficiency, resulting in high AAV vector yield/m^2. Significantly higher yields can lead to fewer required runs, which may result in an overall reduction in media usage.

The Ascent FBR's design also allows for the harvest of viable cells, enabling a broad range of cell therapy applications. This feature also allows this same platform to be used for seed train through to manufacturing, thus simplifying the workflow, reducing the number of technologies required to support the overall upstream process, and providing true scalability across a range of capacities from 1 m^2 to 1,000 m^2. Collectively, these benefits may help drive faster development time to production and significant savings in manufacturing costs.

The Corning Ascent FBR system is designed to offer high-yield and scalability that consistently delivers production volumes with a simplified, cost-effective workflow.

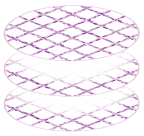
Uniform Fluid Flow

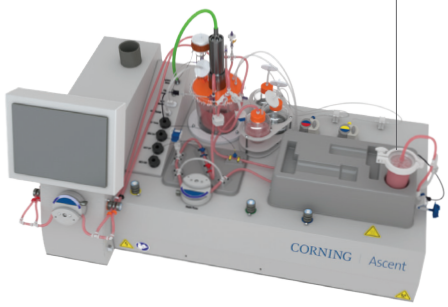
Efficient nutrient delivery and waste removal thoughout bed



Uniform Cell Growth

Optimal distribution and confluence at transfection





True Scalability

The Ascent FBR system is designed to scale from Process Development to Production.

How it Works

The Ascent FBR System is designed around a single-use bioreactor supported by a media conditioning vessel and other accessory consumables, monitored and controlled by an innovative biocontroller.

The Bioreactor

The Ascent FBR System's bioreactor features a specially treated and packed polymer mesh that enables uniform, low-shear fluid flow through the bioreactor bed, which promotes evenly distributed cell growth and enhances exposure of cells to nutrients and reagents. Bioreactors will be available in multiple surface area sizes to provide scalability from 1 m^2 to 1,000 m^2.

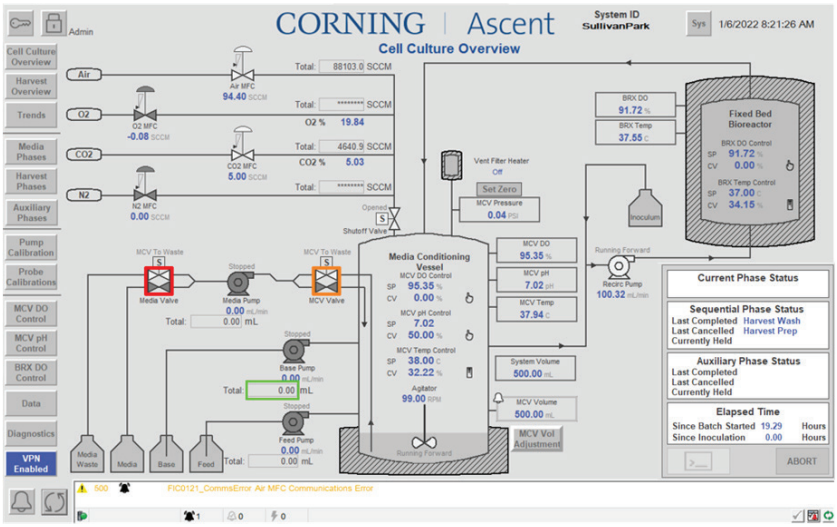
	Surface Area		
Bed Height	**PD System**	**Pilot System**	**Production System**
4 cm	1 m^2 	20 m^2 	200 m^2 
10 cm	2.5 m^2 	50 m^2 	500 m^2 
20 cm	5 m^2 	100 m^2 	1,000 m^2 

The Media Conditioning Vessel

The Ascent FBR System utilizes a separate conditioning vessel, which enables flexibility in managing media conditions and developing optimal processes within the platform. The system's consumable set is equipped with disposable sensors for key process parameters (pH, dissolved oxygen, temperature). All fluid-contacting components are pre-assembled and irradiated; no autoclaving is required.

The Automated Controller

The system controller with Human-Machine Interface (HMI) touchscreen display allows the user flexibility to operate the system in manual or automated modes. During cell culture, a recirculation pump circulates media from the MCV through the bioreactor. A separate pump aids in removing depleted media from the MCV and replacing it with fresh media during media maintenance. Cell culture pH and nutrient levels are monitored and maintained via feed and base pumps while temperature is kept constant. At harvest, cells can be released or lysed in situ from the bioreactor.



Features and Benefits

Features	Benefits
Specially treated woven mesh polymer substrate	• Uniform fluid flow – efficient nutrient delivery and waste removal • Uniform cell growth – beneficial cell distribution and confluence at transfection • Improves cell health and product yield
FBR designed to harvest viable cells with >90% recovery	• Enables its use in other application workflows that require cell recovery for downstream use • Enables the bioreactor to be used for seed train, streamlining vessel-to-vessel cell transfer
Bioreactors scale from 1 m^2 to 1,000 m^2	• Consistent platform from process development to production size can save process development time/cost (reduced time to market)
Separate media condition vessel (MCV)	• Provides flexibility in media volume and dilution strategy for transfection reagents prior to addition
Automated control, including disposable sensors monitor DO, pH, temperature	• Reduced labor costs, hands-off operation, reduced risk of human error
Closed system, ready to use, irradiated consumables	• Minimal set up required, no autoclaving necessary, no probe calibration required. The minimum set up required can save many hours of valuable time.

Uniform Fluid Flow

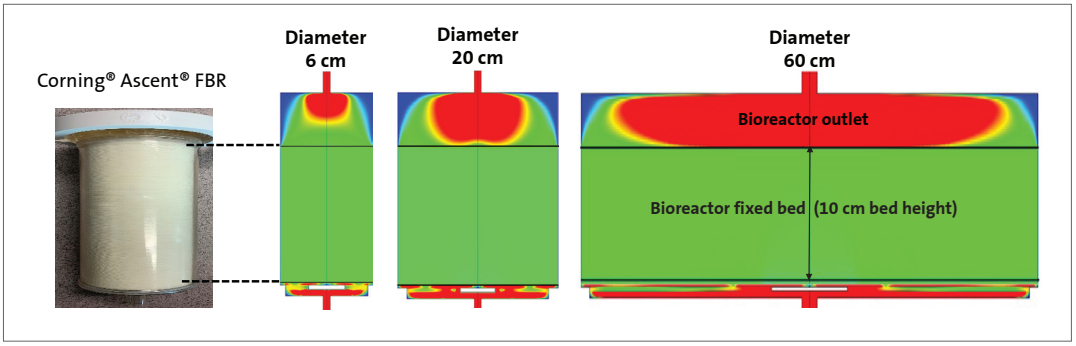
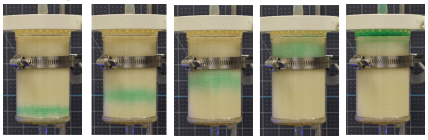


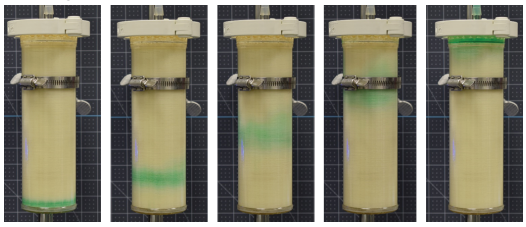
Figure 1. Computational Fluid Dynamics (CFD) modeling for different scale prototype vessels with 10 cm packed bed height shows low shear and uniform flow across a large variation of packed bed diameters.

Residence Time Distribution (RTD) Test Confirms Uniform Fluid Flow through the Corning® Ascent® FBR System

Corning Ascent FBR 2.5 m²

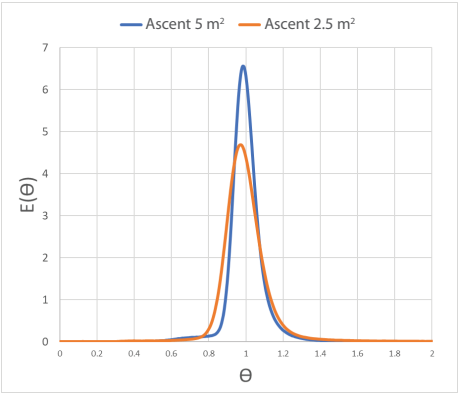


Corning Ascent FBR 5 m²



Flow rate: 100 mL/min.

Uniform RTD Peak Represents Uniform Fluid Flow

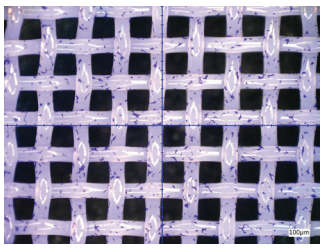


Θ represents the number of reactor volumes of fluid that have flowed through in time *t*.

Figure 2. The final calculated E(Θ) or Θ are dimensionless (normalized parameters) which are independent of vessel volumes or flow rates. Flow rate = 100 mL/min. Θ = 1 and *t* corresponds to approx. 4.6 min. for 5 m² vessel and approx. 2.4 min. for 2.5 m².

Uniform Cell Attachment and Growth

A



B

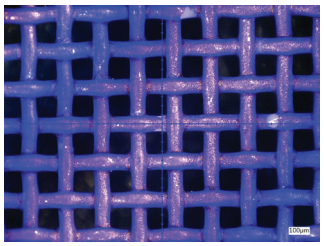


Figure 3. The woven mesh that makes up the substrate in the Corning Ascent FBR enables uniform cell adhesion and growth of cells. In these images (magnification = 100 µm), crystal violet staining of HEK293T cells reveals uniform cell seeding after three hours (A) and subsequent even cell growth after 3 days (B).

Efficient Cell Harvest

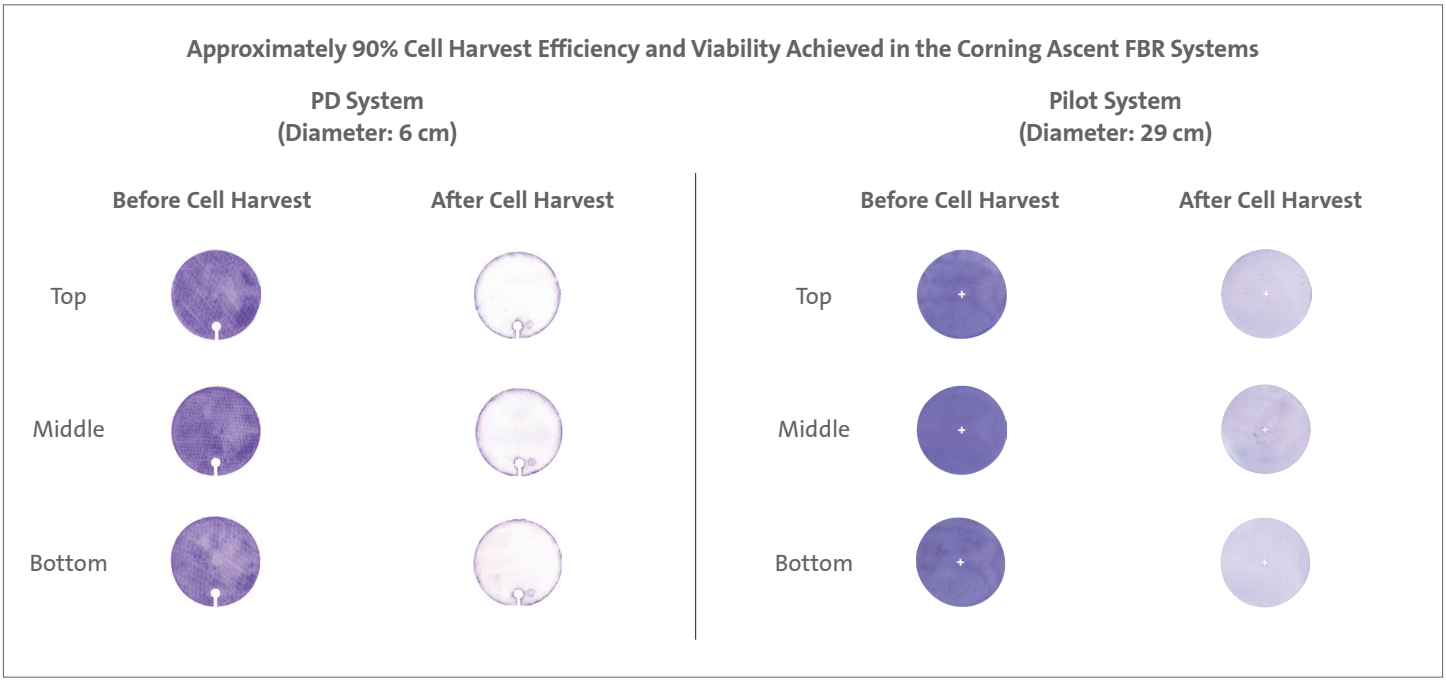


Figure 4. Crystal violet staining shows that cell distribution is uniform across each disk as well as throughout the top, middle, and bottom of the bioreactor in both PD and Pilot systems. Efficient cell harvest is also shown.

Uniform Transfection Across the Bioreactor

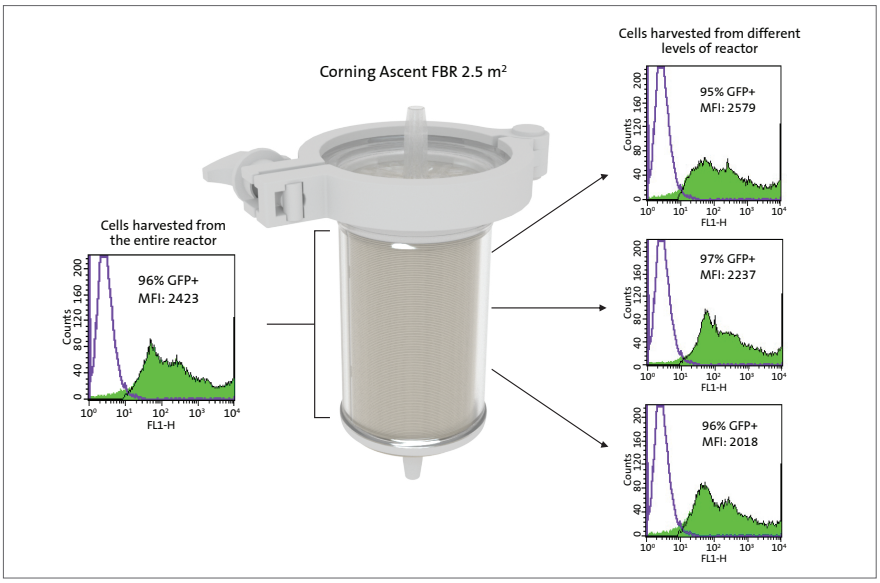


Figure 5. The Corning Ascent FBR has achieved uniform transfection efficiency across a 2.5 m^2 packed bed reactor transfected with AAV2-GFP plasmids. Average % of GFP+ cells was 90.9. (Flow cytometry data are 72 hrs. post-transfection).

Improve your Production Yields with the Corning® Ascent® FBR System

From process development to manufacturing, you can scale-up production of adherent cells and cell products (e.g., viral vectors) in a single, consistent technology platform. The Ascent FBR System is designed to deliver:

- Potential cost savings: With high yield per cm^2, production will require fewer runs to achieve the same quantity of viral particles. Additional savings may result from lower consumption of media and serum/m^2 as well as reduced downstream processing time and waste.
- Viable Cell Harvest: Recover cells for capture of cell-associated viruses, seeding into larger reactors, and a path to cell therapy workflows.
- Reduced CapEx and labor costs: Easy set up, self-contained closed system with irradiated consumables—laminar flow hood not required for operation.
- Uniformity and Scalability: Bioreactors range from 1 m^2 to 1,000 m^2, designed for efficiency.

For additional information or to request a demonstration, visit **www.corning.com/AscentFBR** or contact your local Corning Account Representative.

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