Simplifying Progress

Pionic® Spin: The Innovative Solution for Continuous Virus Inactivation

Lisa Lipski[1*], Karolina-Meyer Heinrichs[1], Stuart Tindal[1], Tobias Steinwedel[1], Johannes Wortmeyer[1], Chad Varner[2], Akshat Mullerpatan[2], Michael Coolbaugh[2] and Kevin Brower[2]

[1]Sartorius Stedim Biotech GmbH, Germany
[2]Global CMC Development Sanofi, USA
*Corresponding author: lisa.lipski@sartorius.com

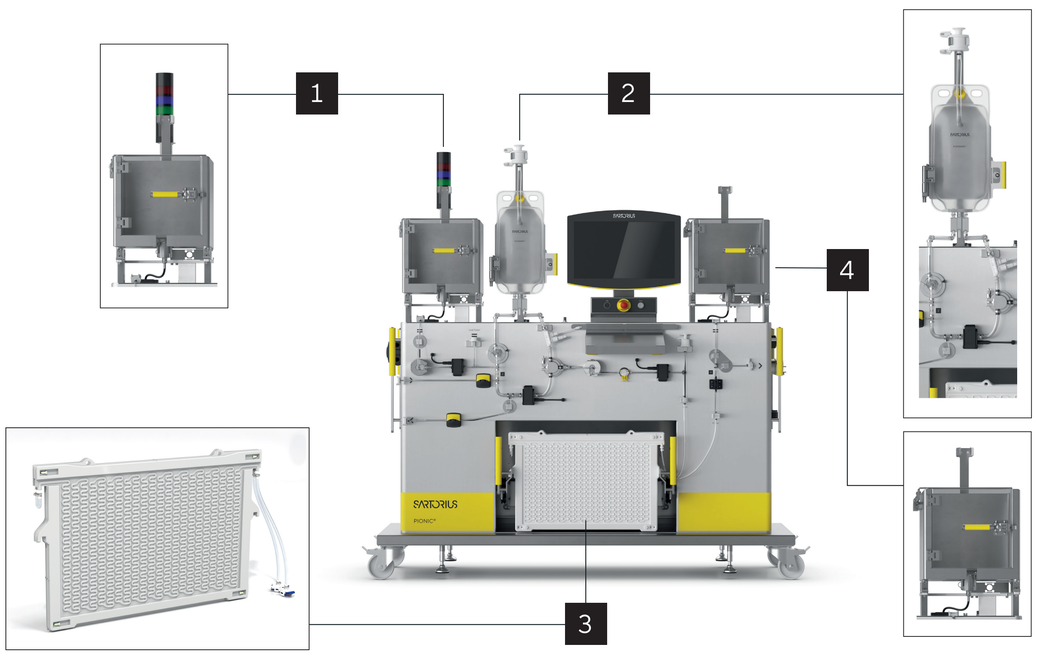
Introduction

Virus inactivation (VI) is a critical step in the downstream processing of active pharmaceutical ingredients (APIs), typically positioned between the capture and polishing steps. According to regulatory authorities, VI is a critical process that reduces active viruses, thereby minimizing the risk of viral contamination in the final product and ensuring patient safety.

Pionic® Spin intensifies VI by enabling the autonomous operation of continuous and robust virus inactivation at low pH. It is specifically designed for long-term perfusion-based processing allowing continuous operation for up to 28 days. Automated inflow pH titration of the incoming feed is carried out in a single step, allowing a control accuracy of ± 0.1 pH.

Pionic® Spin Incubator features a serpentine design that ensures a uniform residence time of at least 30 minutes for low pH incubation. It achieves a reduction of active viruses by ≥ 5 log reduction values (LRV), effectively minimizing the risk of viral contamination in the final product and complying with regulatory standards for VI.

The Four Functional Zones of Pionic® Spin



Homogenization	Acidification	Inactivation	Neutralization
1	2	3	4
Use of a 20 L integrated mixing bag for elution peak cut blending and flow rate balancing	Low-volume recirculation mixing loop for homogeneous acid addition and robust pH titration	Connection of Pionic® Spin Incubator for inflow incubation with narrow residence time distribution	Use of a 20 L integrated mixing bag to prepare the solution for polishing step

Figure 1: *Pionic® Spin With Its Four Functional Zones: [1] Homogenization of the Incoming Feed, [2] Acidification of the Homogenized Solution, [3] Continuous Virus Inactivation, and [4] Neutralization*

Precise pH Control With Integrated Disturbance Control

Precise and rapid pH titration to a specific low pH setpoint is essential for process effectiveness. Pionic® Spin features a novel pH control strategy, including both disturbance control and feedback mechanisms.

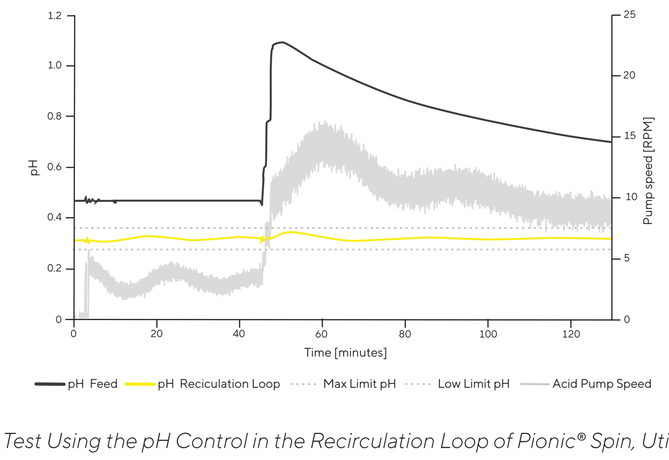


Figure 2: *Disturbance Test Using the pH Control in the Recirculation Loop of Pionic® Spin, Utilizing the Novel Control Strategy With Integrated Disturbance Control*

Three sensors, positioned in the homogenization bag, the recirculation loop, and the neutralization bag, continuously monitor the pH values. For acidification, the disturbance control constantly calculates the difference in pH between the incoming eluates in the homogenization bag and the low-pH target setpoint. Taking into account the titration characteristics of the eluates and other process values, the system determines the appropriate amount of acid to adjust the incoming feed material to the acidic target pH setpoint. The residual pH difference is eliminated using the feedback PID controller, which relies on the pH measurement within the recirculation loop. Both values are set off against each other, resulting in the control value to adjust the acid pump speed. The same control strategy is applied to the neutralization step.

Ensuring Reliable and Precise Incubation Time With Pionic® Spin Incubator

Pionic® Spin Incubator is a cutting-edge single-use device engineered to enhance VI within intensified continuous bioprocesses. It ensures a minimum residence time of 30 to 40 minutes and supports process flow rates ranging from 1 to 22 liters per hour, operating effectively at viscosities between 1 and 3 mPas.

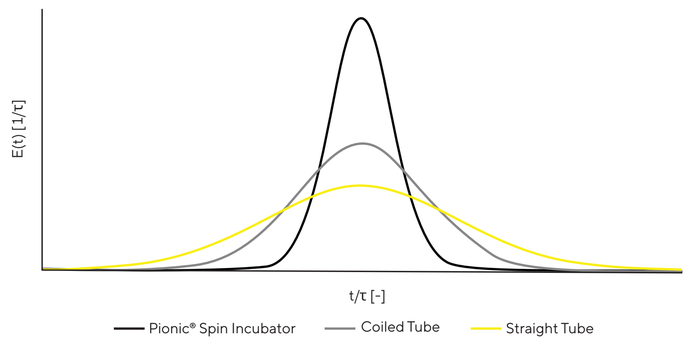


Figure 3: *Schematic Representation of the Narrow Residence Time Distribution of Pionic® Spin Incubator Compared With a Coiled Tube and a Straight Tube Based on the Parabolic Velocity Profiles*

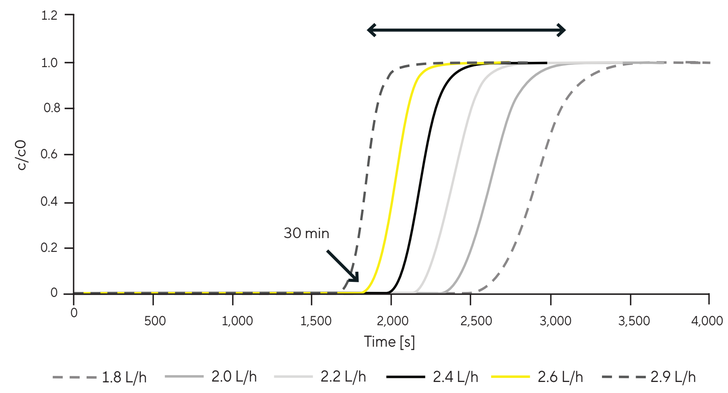


Figure 4: *Residence Times of a UV Tracer in 1.4 L Pionic® Spin Incubator at Different Flow Rates Highlighting the Recommended Flow Rates for the Operation of This Specific Incubator Configuration*

The incubator's curved design facilitates the formation of Dean vortices in laminar flow, promoting radial mixing of the fluid and hence a narrow residence time distribution. Additionally, the device is engineered to minimize the pressure drop across the fluid channel's entire length.

Preview of Longterm Application Results

The effectiveness and functionality of Pionic® Spin in continuous VI was assessed in a 28-day long-term run. The system was operated with a Pionic® Spin Incubator suitable for a 2.4 L/h operation mode to achieve a minimum 30 min target residence time.

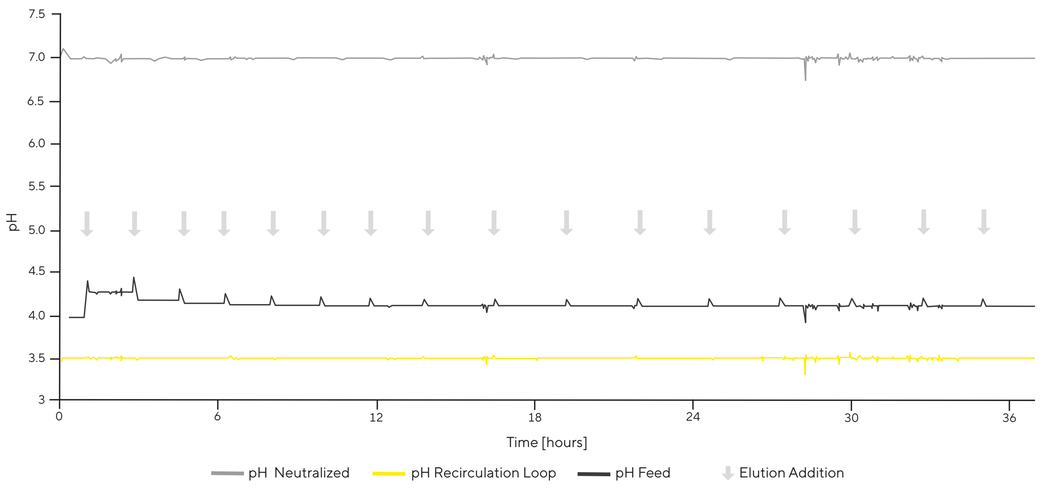


Figure 5: *pH Values in the Recirculation Loop (Yellow Line) and the Homogenization Bag (Grey Line) Are Maintained With Pionic® Spin During a CVI Run Over 36 Hours With Feed Influx (Black Line) From 16 Chromatography Cycles (Gray Arrows)*

Conclusion

Pionic® Spin system helps to intensify bioprocesses and improve efficiency by turning a cyclic eluate flow into a continuous steady state flow through to subsequent polishing steps in clinical or small-scale commercial manufacturing.

Take home message

- In-flow pH Titration
- Adjustable Residence Time
- Operational Time ≤ 28 days
- Inactivation of ≥ 5 LRV
- Digital Communication
- Scalable
- Multi-use System
- Integration DCS Platforms