# REAL-TIME LIVE VIRUS QUANTITATION TO OPTIMIZE PRODUCTION AND MINIMIZE WASTE

## VIRUS QUANTITATION BY LASER-FORCE CYTOLOGY™ OF BIOREACTOR SAMPLES

NIIMBL® The National Institute for Innovation in Manufacturing Biopharmaceuticals

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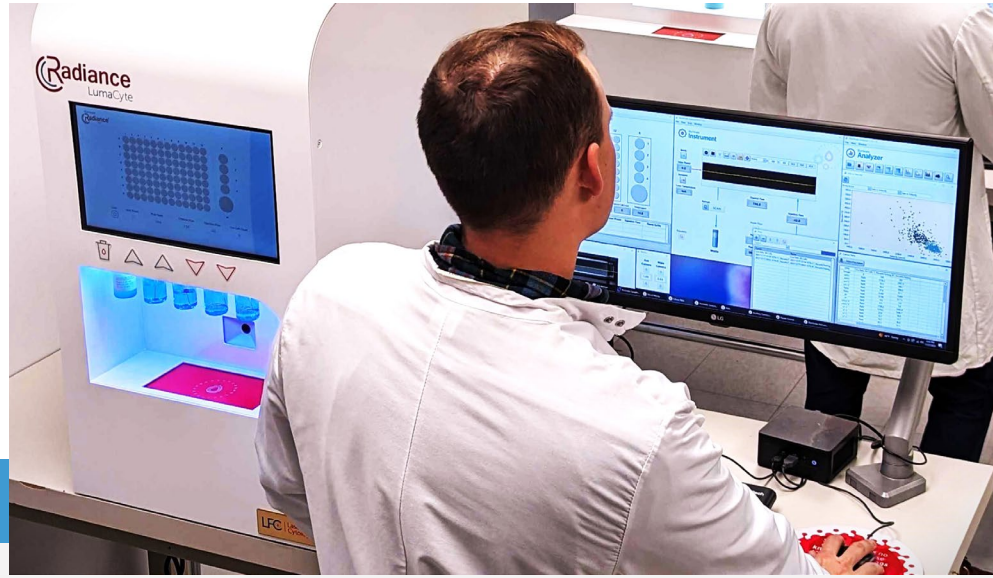


## INDUSTRY NEED

In the biopharmaceutical industry, the urgent need for rapid and sensitive virus detection during the production of viral vaccines has become increasingly critical. Current methods to quantify functionally active virus capable of infecting a cell (viral titer)—such as TCID50 and plaque assays—are time intensive, labor intensive, error prone, and highly subjective. With these current assays, the cost of viral contamination events can be in the hundreds of millions of dollars due to lost product, lost sales, and ultimately a shortage of drug supply to the patients who need it most. For live virus vaccines, regulators have called for real-time, objective, in-process analytics to reduce variability and ensure product safety and consistency. New methods that are capable of more rapid but still broad, sensitive detection of virus are highly desirable, providing the potential to reduce out-of-specification events that lead to batch failures, thereby saving time and costs.

## SOLUTION

Working closely with Merck, the team set out to measure viral titers from three angles. LumaCyte's Radiance® instrument, which leverages an advanced optical and microfluidic technology called Laser Force Cytology™, has the ability to analyze and measure changes in various physical and chemical properties induced by infectious virus at the single-cell level, including optical force, shape, and stiffness. Here, LumaCyte applied the LFC™ method to adherent cells on microcarriers for use in viral vaccine production culture processes, precisely quantifying the amount of functional virus in bioreactor samples in a fraction of the time needed by current assays. To confirm the identity of the virus in the bioreactor sample, Dr. Schneider at Carnegie Mellon developed a method of capillary electrophoresis using genetic probes that bind to specific viral genomes and produce a detectable shift in the sample. Finally, team members at RPI utilized bioreactor data to develop mathematical models to predict the number of uninfected, infected, and dead cells in the bioreactor at any point in the production process.

## OUTCOME

Merck invited the team to their facility to quantify infective, fluorescently tagged measles virus in bioreactor samples. The team produced a working prototype that could measure viral titer in bioreactor samples in minutes, compared to several weeks with viral culture, producing results that correlated with existing assay results.[1] Capillary electrophoresis accurately detected functional virus down to femtomolar levels. Ultimately, the team envisions that virus and cells sampled from the bioreactor could be analyzed in real time in two separate streams, one to measure the quantity of virus and the other to measure virus infectivity.

[1] McCracken, R., Al-Nazal, N., Whitmer, T., Yi, S., Wagner, J. M., Hebert, C. G., Lowry, M. J., Hayes, P. R., Schneider, J. W., Przybycien, T. M., Mukherjee, M. (2022). Rapid in-process measurement of live virus vaccine potency using laser force cytology: Paving the way for rapid vaccine development. Vaccines, 10, 1589. http://doi.org/10.3390/vaccines10101589

> *"Our project demonstrated that NIIMBL is nimble. It brought together partners to identify and pursue priorities and take the research in the direction that would ensure that industry needs were met."*

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