Harnessing the Statistical Power of Design of Experiments to Maximize Viral Vector Biomanufacturing Production

The cell and gene therapy (CGT) market size is expected to reach a value of $113.5 billion USD by 2032 [1]. This growth is driven by an expansion of CGT applications from rare diseases to chronic disorders such as cancer [1]. Despite advancements in the CGT space, viral vector manufacturing is a complex process and producing high-quality, stable viral vectors to maintain their long-term stability and efficacy continues to pose a critical manufacturing challenge [2].

A 2023 survey of 30 CGT organizations found that although respondents were generally optimistic about the commercialization potential of CGTs, 40% lacked confidence in their current manufacturing capabilities to meet demands over the next two to three years [3]. Scaling manufacturing was cited as a critical hurdle, limited by the need for more access to inputs, the absence of standardized or proven manufacturing technology, and inflated cost of or limited access to capital. Therefore, given the capacity challenges faced by the industry, even a modest increase in yield may go a long way in improving manufacturing capabilities. As such, CGT companies must adopt an agile biomanufacturing strategy to maximize the potential of their therapeutic pipeline.

A critical element that impacts viral vector manufacturing yields, that is oftentimes underappreciated, is the innate cellular defenses [4]. For example, HEK293 cells are widely used for viral vector production due to their ease of transfection and low levels of exogenous DNA sensors. Despite this, HEK293 cells still upregulate innate immune response genes when producing viral vectors, suggesting they are not completely neutral to the production process [5] and have an impact on product yield and quality [4].

When you marry the speed of Virica's high-throughput assay with the statistical approach of DoE and bridge the two strategies with an automation software platform, we can leverage this combined computational power to program our liquid handlers to perform the experiments and get feedback extremely quickly. These three key pieces represent an innovative approach that has kicked our offering into high gear.

Jean-Simon Diallo
Scientific Founder and CEO

Virica's High-Throughput Virology Approach to Targeted Screening

At Virica, our aim is to help clients make therapeutic viruses grow and work better by reducing these innate cellular defenses through our viral sensitizers, or VSE™ platform. Virica leverages liquid handlers and dispenser robotics to develop high-throughput production and quantification assays. Small scale 96-well production allows us to harvest crude samples, transfer vectors into reporter cells, and quantify functional vector production.

Virica's virology expertise, product portfolio, and workflows deliver a 2-5x increase in viral productivity, improves quality metrics, and transduction efficiencies (based on application). Our approach has been tested in over 50 applications and combinations of cell and viral products. Additionally, VSE™ deliver a 30-50% reduction in manufacturing costs, which represents a critical barrier to access to potentially life-saving therapies [6].

The power of identifying key drivers and the speed with which you can get these answers and how quickly you can optimize cost-for dose is a key aspect of our DoE approach. We can support your product development across the entire life cycle, from the early ideation stage where yield might be the most critical factor to strategies that minimize cost per dose as you move into the clinic.

Jondavid de Jong
Vice President, Scientific Operations

Harnessing Statistical and Computational Power to Rapidly Optimize Your Process

We have taken our proven high-throughput platform developed from years of research experience and VSE™ development to create screening panels unique to Virica. To further build on our proven expertise in accelerating viral vector productivity, we have coupled our platform with the statistical power offered by Design of Experiments (DoE) to deliver more cost-effective approaches to optimize your production processes. Our previous methodology applied the conventional "one factor at a time (OFAT)" experimental approach, which tested factors that influenced the productivity of viral vectors (i.e., cell viability, virus output) within a restricted experimental space (Figure 1). With the DoE approach, we can capture synergistic and additive interactions of variables and parameters that could further optimize viral outputs.

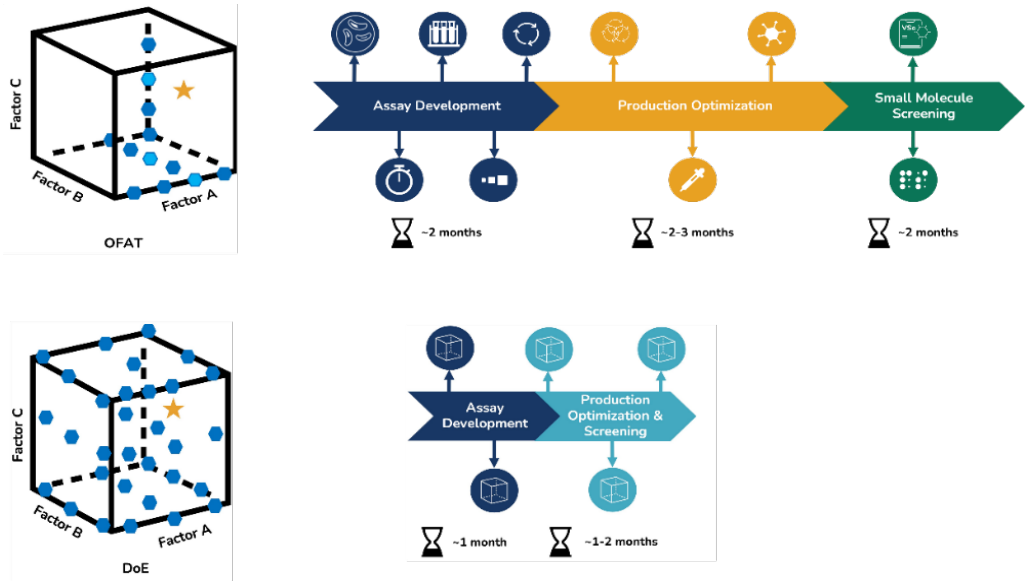

Figure 1: Harnessing the potential of DoE. (A) The OFAT is the traditional scientific approach to experimentation and limits the experimental space. (B) DoE is a systematic and efficient method of experimentation that enables explorations into a complex experimental space to investigate unknown interactions that may maximize production processes, thereby increasing cost-effectiveness.

By coupling the statistical analysis of DoE with an automation software platform, we can unlock otherwise unknown interactions and parameters critical to the production of viral vectors, thereby accelerating our screening process to accomplish two key goals:

1) Identify fit-for-purpose VSE™s for specific applications including adeno-associated viruses or lentiviruses.
2) Offer agile modelling approaches to support a client's upstream manufacturing of CGTs while maintaining flexibility to adjust these parameters at scale.

Our unique application of DoE allows us to not only test parameters of value to our clients (i.e., plasmid ratios optimization, transfection reagents), but also identify variables that may not have been considered from a cost-reduction perspective. Notably, key drivers can be further modified at the scale-up stage and can enable cost-effectiveness and maximize resource usage as fewer factors and variables will need to be tested at the scale-up stage. Our innovative approach can effectively reduce development timelines and minimize hands-on time, ensuring rapid optimization of your process.

The DoE approach has the capacity to answer nearly all questions that our customers have, we just have to frame it the right way. We're an additive company, meaning we are integrated into various platforms at various points. DoE has let us leverage our technology the best we can for each use case by assessing a wholesome view of any unique process.

Keara Sutherland
Scientist

Final Thoughts

The comprehensive understanding of countless parameters that will impact productivity and scalability of viral vectors offers a strategy that not only serves to maximize total yield of viral vectors but also reduces manufacturing costs.

Virica's clients are now able to unlock the full potential of their viral vector production process with the innovative application of the DoE to Virica's high-throughput assay. It is now possible to achieve rapid optimization of multiple factors, thereby saving time, resources, and effort. With this approach, our clients gain unparalleled flexibility and deep insights into key production parameters by embracing DoE and can discover optimization possibilities never thought possible.

We are excited to offer our high-throughput virology powered by DoE to help clients revolutionize their manufacturing efficiency and outcomes.

Keywords: Virica Biotechnology, viral vector biomanufacturing, high-throughput assay, viral sensitizers, design of experiments, adeno-associated viral vectors

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