The Value of Peptones for Cost-Effective Vaccine Manufacturing

Vaccine manufacturing is a complex and highly regulated process, requiring precise control over cost, productivity, and timelines.

To achieve commercial success, biopharmaceutical manufacturers must overcome challenges of supporting consistent yields, maintaining process efficiency, and navigating supply chain uncertainties. Peptones — versatile protein hydrolysates that can represent helpful additives for a range of bioprocesses — offer a strategic solution to many of these challenges. They can provide important nutrients that enhance cell growth, improve process robustness, and drive higher vaccine yields.

One of the key advantages of peptones lies in their ability to reduce overall production costs. By improving cell culture performance, peptones help manufacturers achieve greater efficiency, ultimately making vaccines more affordable and accessible. Their role in enhancing cell viability and productivity can also contribute to high-quality production, potentially improving batch-to-batch variability and helping to reduce the burden of quality control.

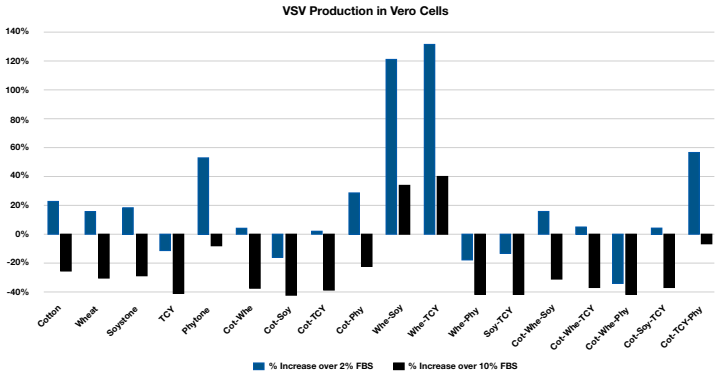
Speed-to-market is as crucial a factor as any in successful vaccine development. With increasing global demand and evolving regulatory expectations, rapid process optimization is important. Peptones support faster development timelines by promoting cell health, extending culture viability, and enhancing specific productivity, allowing manufacturers to accelerate production while maintaining stringent quality standards.

Composed of free amino acids, peptides, proteins, and important minerals, peptones act as a powerful nutritional source that supports optimal cell growth and function. Their protective effects, including buffering against toxic media components and delaying apoptosis, contribute to improved cell culture performance, ultimately leading to higher vaccine yields. By integrating peptones into vaccine bioprocessing, manufacturers can address critical industry challenges, thereby improving cost efficiency, supporting process consistency, and potentially expediting production timelines.

gibco

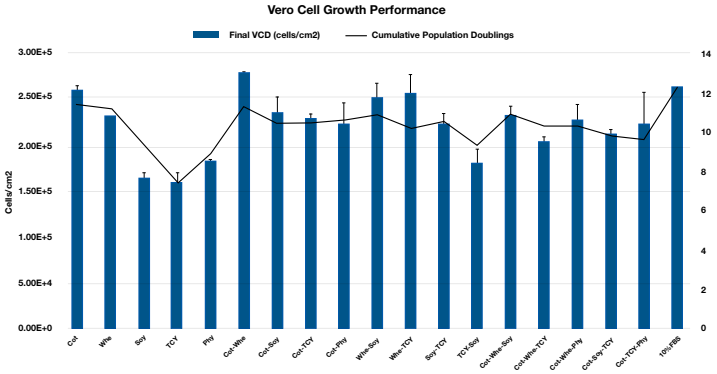
Peptones and Adherent Vero Cells: An Evaluation of Cell Growth and Virus Production

In two separate case studies, scientists at Thermo Fisher Scientific set out to demonstrate the value of peptones for reducing serum usage while improving virus production in Vero cell cultures. In the first case study, researchers evaluated the impact of animal-origin free (AOF) Gibco™ peptones on adherent Vero cells, the most widely used adherent cell line for both human and animal viral vaccines. Five distinct AOF peptones were evaluated as part of the study — Cotton, Wheat, Soytone, Phytone, and TC Yeastolate — alongside several peptone blends that offer expanded nutritional profiles to determine the best feeding strategy.



Vero cells were cultured in media containing various animal origin-free (AOF) peptones, either individually or as blends, at a concentration of 4g/L, supplemented with 2% fetal bovine serum (FBS) with 10% FBS condition as control. Prior to assessing cell growth and virus production, the cells were adapted to these peptone-containing media. They were then infected with vesicular stomatitis virus (VSV) at a low multiplicity of infection (MOI) of 0.0001. Virus titers were subsequently quantified using plaque assays, and the percentage change measured for VSV titers in the peptone-containing, reduced-serum media was compared to control conditions; all experiments were conducted in triplicates.

The data generated by Thermo Fisher was able to demonstrate comparable cell growth for many of its peptone combinations against the control. It was likewise able to achieve an 80% reduction in serum. This represents a valuable compromise for applications for which serum-free media cannot adequately supplant traditional approaches, as well as an important value-gain through reduced supply chain costs.



In particular, the study found that certain peptone blends, such as Cotton-Wheat, Wheat-Soytone, and Wheat-Yeastolate, performed as well or better than the control. These results demonstrate that peptones can be combined and calibrated to optimize processes and reduce reliance on serum with comparable results.

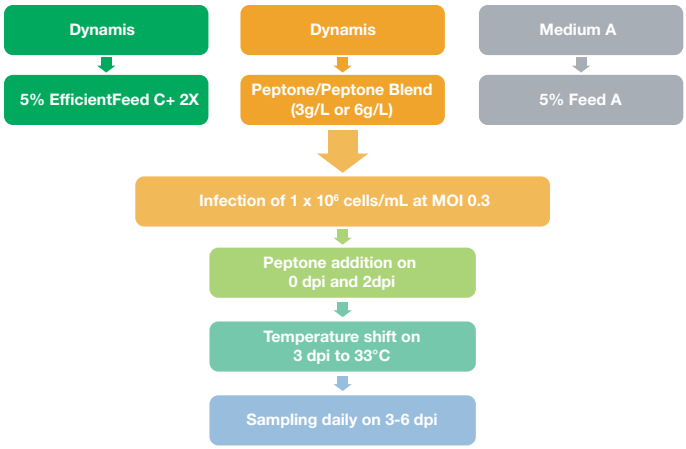
In the second case study, researchers evaluated the impact of peptones on suspension HEK293 cell cultures. Because the vast majority of suspension cell cultures are serum-free, the study evaluated whether AOF peptones could boost cell growth and virus production for these applications. AOF peptones (2 or 6 g/L) — individually or as blends — were supplemented as single fed batch at the start of study, and both HEK293 and BHK-21 cells were cultured in Dynamis (Gibco™) and CD BHK (Gibco™) media, respectively. The following findings were observed:

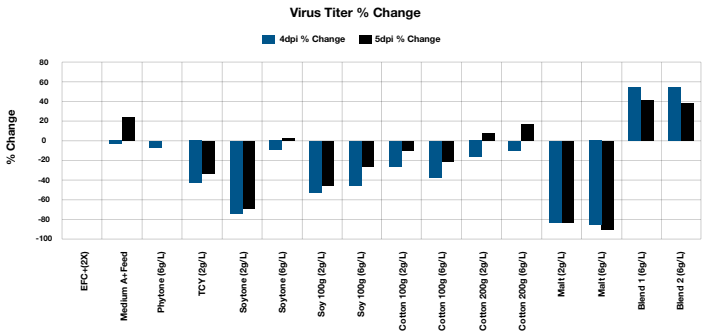
- Increased Cell Density: Supplementing media with peptones (Yeastolate, Phytone, or a 50/50 blend) significantly increased peak viable cell density (VCD) in both suspension HEK293 and BHK-21 cells compared to control media.
    - HEK293: 10-30% increase in VCD with peptone supplementation.
    - BHK-21: Up to twofold increase in VCD with peptone supplementation.

Scientists likewise looked at virus production in cell cultures supplemented with various peptones; in its study, Adenovirus 5 production was evaluated with a control that utilized 5% EfficientFeed C+ 2X, a Gibco media proven to improve Adenovirus 5 production. Results of this evaluation found:

- Variable Results: Individual peptones did not consistently improve adenovirus 5 production compared to the control.

- Peptone Blends Effective: A blend of TCY and Phytone (both 75:25 and 50:50 ratios) resulted in up to a 50% increase in adenovirus 5 virus production.





For each run, AOF peptones (2 or 6g/L) — individually or as blends — were supplemented as fed batch twice (1hpi and 2dpi). Cells were cultured in media only for all conditions, and then, once a culture reached 1 x 106 cells/mL, it was infected at a low multiplicity of infection of 0.3 viruses per cell; at one-hour post-infection, all cultures were fed with either the control media or peptones. An additional competitor media was evaluated and fed twice, first one-hour post-infection and again after two days.

Ultimately, it was shown that, while most peptones did not provide improvement on their own, two blends using Yeastolate and Phytone peptones yielded a nearly 50% increase in Adenovirus 5 production on Days 4 and 5. This study highlights the need for careful evaluation of different peptone types, blends, and concentrations to optimize virus production for specific processes.

Effectively Incorporating Peptones for Optimal Biomanufacturing

Peptones, while beneficial components in biopharmaceutical manufacturing, are often perceived as inherently variable, potentially jeopardizing process consistency. This perception stems from their biological origin, leading to concerns about lot-to-lot inconsistencies. However, Thermo Fisher has dedicated significant resources to understanding and mitigating this variability, supporting reliable performance with their Gibco™ peptone portfolio. By meticulously analyzing the sources of variability and implementing robust control measures, Thermo Fisher empowers manufacturers to achieve consistent and predictable outcomes in their bioprocesses.

Thermo Fisher addresses peptone variability through a dual approach. Firstly, stringent vendor requirements and rigorous internal controls are implemented to support the quality and consistency of raw materials. This includes meticulous selection of raw materials, comprehensive analytical testing to identify potential sources of variability, and the utilization of advanced analytical capabilities across the Thermo Fisher network. Thermo Fisher Scientific also offers custom and catalog SKUs, allowing customers to precisely control critical parameters.

Next, Thermo Fisher focuses on process-specific requirements, recognizing that different Gibco peptones exhibit varying performance characteristics across diverse applications. To optimize performance, Thermo Fisher offers a wide range of peptones and provides analytical and Key Driver Identification (KDI) services. The KDI services leverage its extensive technical expertise in cell culture and vaccine manufacturing to pinpoint critical variability drivers and develop tailored solutions. Moreover, their broad cell culture experience enables effective troubleshooting and problem-solving, facilitating the integration of Gibco peptones into manufacturing processes.

Its secondary strategy prioritizes a key driver identification (KDI) approach, designed to identify critical peptone components influencing process performance. This approach moves beyond the traditional “test and hold” method, which relies on evaluating multiple lots and hoping to find suitable material. The KDI service instead utilizes a sophisticated model to analyze customer-provided data and internal analytics, identifying key drivers that positively or negatively impact process outcomes. By pinpointing these drivers, Thermo Fisher can develop custom SKUs with precisely defined specifications, supporting consistent performance and eliminating guesswork. For instance, a customer experiencing low lot acceptance rates (27%) was subsequently able to achieve 100% acceptance after implementing a custom SKU developed using the KDI approach.

The KDI process itself is a data-driven and robust approach. It begins with the collection and analysis of customer-provided data and internal analytics to understand process performance and identify potential key drivers. This data is then used to build a model that predicts the impact of specific analytes on process outcomes. Through iterative testing and refinement, the process narrows down a wide range of potential analytes to a specific specification range, supporting optimal performance for the customer's application. Finally, the optimized specifications are integrated into the manufacturing process, utilizing validated analytical models to support consistent product quality with every order.

In conclusion, Thermo Fisher's Gibco peptones, supported by rigorous quality control and an innovative KDI service, provide a reliable solution for biopharmaceutical manufacturers seeking consistent and predictable process outcomes. By understanding and mitigating the inherent variability of peptones, Thermo Fisher empowers customers to optimize their processes, reduce costs, and accelerate time to market. This is especially critical in vaccine production, where consistency, scalability, and speed can directly impact public health outcomes. High-quality peptones contribute to robust cell growth and protein expression, helping support the efficacy and safety of vaccines produced at scale.

Learn more at **thermofisher.com**