Peptones: a powerful tool for manufacturing complex protein therapies

Introduction

Peptones have emerged as a valuable media additive for a range of biopharmaceutical applications. They are a heterogeneous mixture of polypeptides, oligopeptides, free amino acids, trace metals, and nutrients derived from various sources, including yeasts, plants, and animals. In contrast to more complex—and consequently, more undefined—additives such as fetal bovine serum (FBS), peptones can offer more consistency for a manufacturing process, a crucial consideration for enabling reproducibility and control.

Peptones possess a number of advantages for a biopharmaceutical workflow. These supplements lack the same potential for risk that researchers can encounter with FBS, and they have achieved improved cell growth and viability alongside lower variability, owing to more consistent processing. Other key benefits of incorporating peptones into a cell culture workflow include:

- Nutritional diversity, with many peptones containing a range of components, including carbohydrates, vitamins, and trace elements, among others
- Nutritional buffering capacity that improves cell health and confers protection from toxicity
- Higher titers and improved protein quality compared to chemically defined processes
- Better cell-specific productivity (Qp), a significant indicator of the efficiency of a cell culture process

The benefits of peptones have already been realized for hundreds of commercially approved applications. Ultimately, these supplements hold promise not only for traditional monoclonal antibodies (mAbs), where they have been proven to improve process productivity and quality, but also for more complex proteins like bispecific antibodies and antibody–drug conjugates (ADCs).

Boosting productivity and efficiency: the power of peptones

The downstream efficiencies enabled by peptones are a key consideration for developers. Their capacity for boosting Qp can allow for more productive manufacturing within the same infrastructure constraints as an existing process, creating significant cost benefits by curtailing the need for additional manufacturing capacity to meet product demand. The nutritional benefits of peptones make them a ready solution for operators in both early- and late-stage process development, allowing them to achieve productivity goals with minimal resource expenditure. Likewise, peptones can be flexibly incorporated into a cell culture process. These supplements can also be used as part of a media strategy wherein various peptones are blended to obtain synergistic effects.

For those working with traditional mAbs and more complex proteins alike, the primary development challenges are linked to achieving target productivity and securing regulatory approval. Because they are newer modalities compared to traditional mAbs, bispecific antibodies and ADCs still have considerable ground to cover in establishing manufacturing paradigms that can achieve the necessary consistency and productivity. The newness of these processes has made some in the space reluctant to explore media components that are not fully chemically defined, as they are concerned about the potential regulatory implications of incorporating undefined additives such as peptones into their workflows.

The possible benefits of peptones for improving the quality and productivity of a process are as true for complex proteins as for any other biopharmaceutical application. These components are widely used in many commercial biopharmaceutical applications, proving their capacity to pass regulatory muster. **Vetting a peptone's suitability** for one of these processes is straightforward. First, developers must choose whether to employ animal origin (AO) or animal origin–free (AOF) peptones. This requires testing all suitable peptone candidates in either category before potentially engaging in titration to narrow down the best candidate, analyzing various concentrations and any potentially beneficial combinations with other peptones.

Although many in the industry have expressed increasing interest in AOF peptones, AO peptones can offer an effective and reliable solution for many cell culture and bioprocessing applications. AO peptones are frequently used to reduce or eliminate the need for serum in some media formulations and can promote strong cell growth and toxin titers for vaccine production. Other considerations, such as the endotoxin level and bioburden of a given peptone, may also drive developers to select an ultrafiltered peptone, particularly for mammalian cell processes.

This evaluation must occur in conjunction with continual testing of the key attributes of a drug substance. Ultimately, focusing on titer alone during early optimization is shortsighted—any change to a media feed has the potential to create a shift in one or more of a drug's key attributes. These shifts, if not monitored during scale-up, can cause out-of-spec results during later development stages, resulting in losses of time, money, and resources. The complexities of both peptones and the protein therapeutics being pursued today make this foundational characterization crucial.

Leveraging peptones for complex biopharmaceutical production

Applications that require an increased focus on cost considerations, such as viral vector gene therapies, may reap additional benefits through incorporating peptones into a media formulation. This is because these nutritionally diverse supplements can enable greater titer gains while incurring less expense than many other raw materials. Moreover, because a peptone can sometimes supplant multiple other discrete additives, operators can simplify their supply chain and streamline workflows, potentially creating added time and cost advantages.

Because the processes used to generate ADCs and bispecific antibodies are more complex than those used for traditional mAbs, there exists potential for additives like peptones to help support improved early development by bolstering the productivity of these applications. While any raw material can introduce the potential for variability in a process, the tight control suppliers have established over peptone production has rendered these materials highly consistent. Peptones have been incorporated into the manufacture of several blockbuster drugs, proving their ability to support scale for products targeting large doses or patient populations.

Transitioning to larger scales for these complex mAbs requires the same focus on sources of variability throughout, but the consistency of the peptones available for bioproduction today makes them a less likely source of variability than many developers may believe. As developers scale up their complex mAbs, lot-to-lot consistency for these processes becomes even more important. Peptones have come a long way over the last 60 years, and manufacturing processes have evolved with the bioprocessing industry to produce peptones with tighter controls and better consistency. It is critical to look at all key attributes for impact based on lot-to-lot consistency, and there are many techniques available to further control for variability in order to arrive at a highly consistent, high-yield workflow.

Conclusion

As the demand for high-quality biotherapeutics continues to grow, peptones, with their comparatively defined composition and more consistent performance, will undoubtedly play an increasingly vital role in the biomanufacturing landscape. These additives, used in more than a hundred commercial products spanning both human and animal drugs in a range of modalities, are proven effective in boosting productivity and quality. Their flexibility, cost efficiencies, and potential for simplifying workflows and supply chains make them a valuable tool for not only complex mAbs but also other emerging biotherapeutics such as cell and gene therapies.

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