Importance of high-performance cell culture media and feeds: an industry perspective

Cell culture media and feeds are an essential part of biopharmaceutical production, playing a central role in determining both process productivity and product quality. As a result, developing formulations that can maximize performance and consistency is critical to enable developers to achieve sustained economic viability and long-term commercial success.

However, developing formulations that can support optimal cell growth and function can present several challenges, particularly for newer modalities. The development workflow itself can also be highly variable, depending on the process type. Consequently, it is essential for developers to understand the latest approaches and next-generation technologies that can be employed to optimize development.

To find out more about the benefits of high-performance cell culture media and feeds, as well as current development challenges and their potential solutions, we spoke to a panel of four Thermo Fisher Scientific cell culture professionals, with experience across a wide range of modalities and process types.

Panelist information

Erica Wehling: Senior R&D manager

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Sonjoy Mukerjee, PhD: Principal application scientist

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Erica, to start us off, could you provide an overview of the benefits that biopharmaceutical manufacturers can gain from using cell culture media and feeds that are optimized for their cell line and process?

Erica: One of the primary benefits for manufacturers is improving their ability to consistently meet their product's critical quality attribute (CQA) requirements. CQAs are fundamental to the efficacy of the final product, so tailoring media to consistently meet them is essential. Another benefit of tailored media is the ability to maximize product titers. Together, this can enable manufacturers to achieve optimal process productivity, thereby potentially reducing their cost of goods sold. More time spent on upstream development can also lead to more simplified downstream processes. For example, by using a medium that promotes optimal cell health, the amount of cell-derived impurities that need to be removed can be reduced. So, getting the medium right early on has massive benefits for the end results.

Given the benefits of using optimized cell culture media and feeds, what do you think are the most common barriers that stop manufacturers from developing high-performance solutions?

Erica: There are a range of barriers; some manufacturers may not have the experience, knowledge, tools, or capacity to handle the project in-house. Timelines are another hurdle to overcome—pressure to maximize speed to market and develop a solution often results in suboptimal formulations.

To look more specifically at different areas of the industry, how would you say media and feed development goals vary across different modalities?

Sonjoy: During media development, the end goals ultimately come down to the therapeutic being produced and the titers required. For example, with biosimilars, meeting the quality profile required for comparability is paramount and titers are less important; while for biobetters and viral vector–based gene therapies, maximizing product titers is a central goal.

Natalie: Leading on from that, within viral vector production, other more specific goals may be to increase transfection efficiency, as well as meet the ideal full/empty capsid ratio. However, for cell therapies, it might be to reduce the number of supplements required and develop a serum-free medium that allows for a shorter T cell expansion time.

Bianca: In my role, I am seeing more of a desire to develop custom media and feeds specific to CHO cells and protein processes. Additionally, with developers working with Sf9 cells, there is a drive toward optimized or chemically defined media. Within the bacterial space, developers are now looking to create fermentation-specific feeds to work alongside their media.

Moving on from modalities, how do the approaches to media development vary across different processes, such as perfusion for example?

Erica: Perfusion has become a popular option when it comes to improving process productivity; however, it does require a different approach to media development. For example, using a representative scaled-down model for design of experiment (DOE) studies is even more essential. Plus, having confirmation checkpoints built into the development workflow to validate formulations as you scale up from bench scale to commercial production is key. And with that, successful conversion of the medium into a dry format is also important due to the higher media volumes required for perfusion processes.

Looking at the challenges of media development, are there any specific areas, either for processes or modalities, where you think high-performing solutions are lacking?

Natalie: Within the cell therapy field, the transition from autologous to allogeneic therapies is creating a big shift right now, alongside a growing opportunity to use natural killer cells—both of which would benefit from optimized media solutions.

Erica: Using perfusion as an example again, having a single medium that can be used throughout the process, from seed train to production, can help simplify manufacturing. However, developing a medium that is robust enough and consistent in performance to achieve this, while also meeting the needs of the culture and maintaining high productivity, can be a challenge for manufacturers.

Sonjoy: New cell types are continually being discovered which, while positive for the industry in a broader sense, can become a problem when trying to tailor media, as every cell type has different needs. On top of this, an increase in intensified processes is resulting in culture times being extended from 14 days to 2 months. This prompts a new challenge—how can we keep a cell type viable and maintain optimal productivity for longer periods of time?

Bianca: I think it is also worth noting that, while there are a variety of options for many CHO cell lines, there are still some that could benefit from more high-performance media solutions, such as CHO-M. Additionally, within the supplementation space, more solutions designed to modulate specific protein quality attributes could be useful for developers.

Thinking about all of these challenges, what approaches or equipment solutions are available in order to minimize and manage the challenges faced in more niche therapeutic areas and process types?

Erica: I think automated, high-throughput systems are very important for media development, as they can enable developers to widen their design space and test more diverse media formulations. On top of that, multi-omics technology is an increasingly innovative area that can provide greater insight into cell lines' nutritional requirements and help developers identify new formulation candidates by offering an understanding of intracellular pathways. Both technologies can help manufacturers reach a more optimized formulation and therefore support the development of a more productive medium.

Bianca: Related to using high-throughput systems, taking advantage of scale-down modeling and working toward the most optimal process on a smaller scale can be highly beneficial. In particular, this approach can enable developers to gain a full understanding of their process in a more time- and cost-efficient way, which can be used to inform media development.

Outside of media development itself, are there any additional strategies that can be applied to help optimize production?

Sonjoy: It is not just media formulations that need to be optimized, but also the feeding strategy. The amount of feed added and the timing of addition is critical. Also, looking into using lean basal media with concentrated feeds can benefit productivity. Some cell lines do not grow well using rich media formulations, so adding more concentrated feeds later in the process can ultimately lead to a higher yield. From a strategic perspective, this is proving to be popular within industry, as it also allows for reduced production costs since less feed is required.

Erica: Related to supplementation, evaluating peptones as a potential option to improve performance can be beneficial. There are a wide variety of peptone supplements available, which can provide many of the key components required for optimal cell culture performance. Moreover, compared to other commercially available supplements, they are relatively inexpensive, making them a powerful option, particularly for cost-sensitive workflows.

Natalie: Process development is another aspect that can help achieve the desired goals. Considering temperature and pH shifts and their setpoints, as well as gassing profiles, could all benefit media development and optimization.

Looking to the future, are you seeing any shifts in the types of challenges that are arising with regard to media and feed development?

Erica: On a broader level, keeping up with the latest technology and novel processes when they are constantly evolving can be challenging. For example, as technology progresses, developers have access to much larger datasets for media development than ever before, which require sophisticated analyses. It can be a struggle for some developers to fully understand how to best use these data for media design.

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Finally, are there any solutions on the horizon that could help developers mitigate current and future challenges during media and feed development?

Sonjoy: Within the cell line development space, there is a growing focus on finding the optimal insertion site for the gene of interest within a cell's genome to enhance production. Also, further advancements in multi-omics analysis could enable a more in-depth understanding of what is driving productivity, by providing new insights into key titer- and quality-influencing pathways.

Erica: I think it comes down to embracing that, for different modality types, different media and feed development approaches may be needed. As we have found, what works when developing media for fed-batch mAb production processes may not translate to viral vector media development. As a result, for developers, keeping up-to-date with the latest innovations and industry best practices is critical to enable them to develop an optimized solution for their process.

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