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Strategies for Optimizing Upstream Processes

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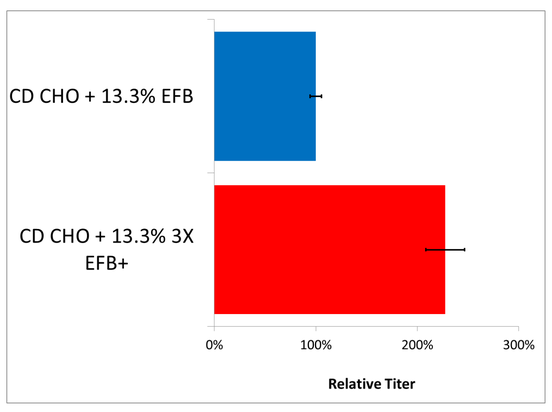
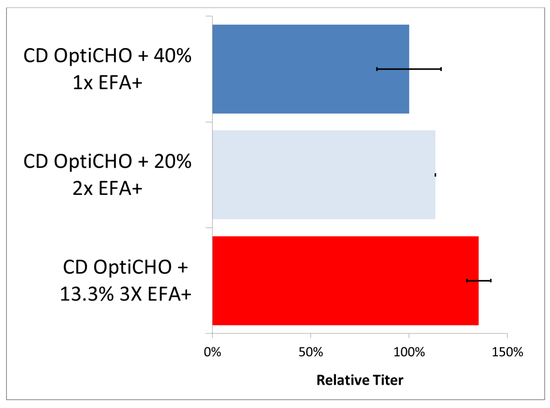
ABSTRACT

The cell culture process is crucial for maximizing the production of biologics and vaccines, as well as optimizing product quality attributes, minimizing impurities, and simplifying operations. Companies employ different strategies based on the business and technical requirements for their desired products. Achieving high cell densities and titers are common goals, but companies producing biosimilars may engage in a strategy that focuses on matching specific product quality attributes, while companies producing a viral vaccine may leverage a strategy the minimizes impurities. A well-defined sourcing strategy that includes use of high quality/purity animal-origin-free components can improve performance and reduce risk. Additionally, companies are seeking to identify opportunities to streamline operations and reduce cost of goods, regardless of the type of product they are producing. This presentation will highlight case studies to demonstrate how optimizing the composition and format of media supports all of these upstream strategies.

Case Study 1: Increasing Titer through Super Concentrated Feeds

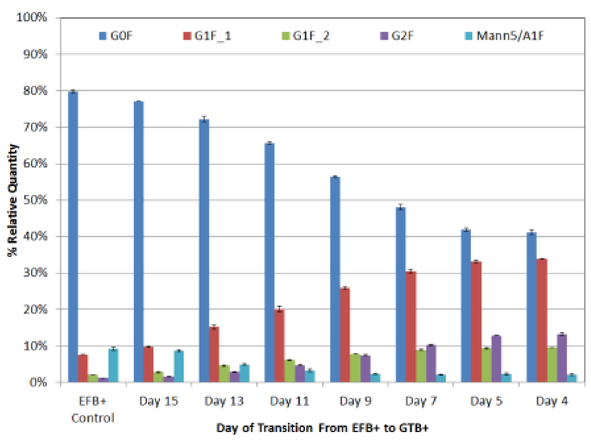


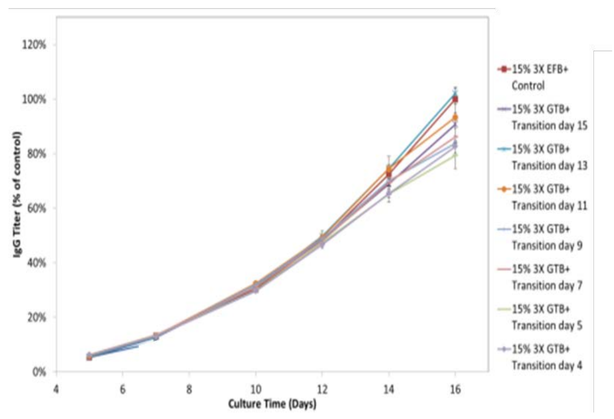


Leveraging super-concentrated feeds can improve bioreactor operations and increase titer:

- Changing feed concentration from 1x to 3x resulted in a **2.3- fold improvement in titer**.
- Reducing feed volume, while increasing feed concentration, resulting in a 35% increase in titer and significantly **less volume fluctuation in the bioreactor.**

Case Study 2: Optimizing glycan profiles through Feed Formulation and Feeding Strategy

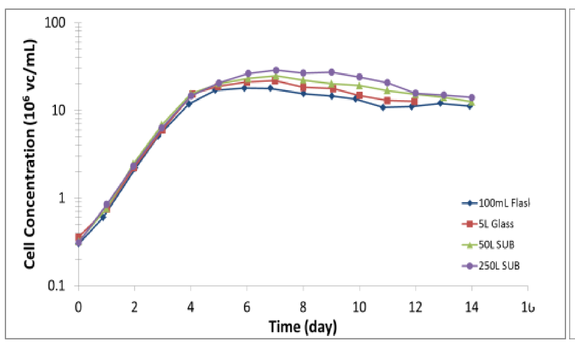


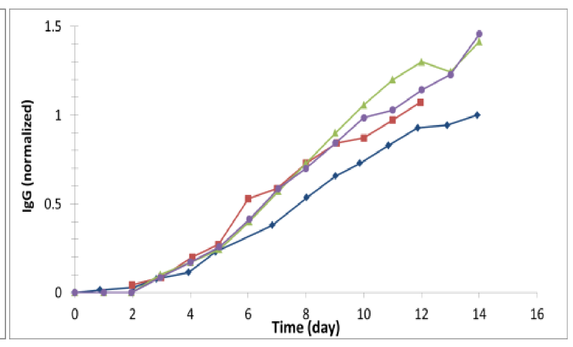


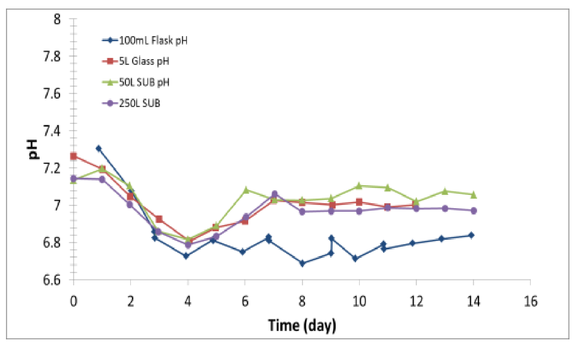
Optimizing the supplementation of key components can redefine protein quality attributes:

- Adjusting the timing of the supplementation enables the **fine-tuning of glycan patterns**.
- Optimizing the concentrations of the supplements **minimizes impact to cell growth and titer**.

Case Study 3: Leveraging pH shift for Consistent Process Scale-up





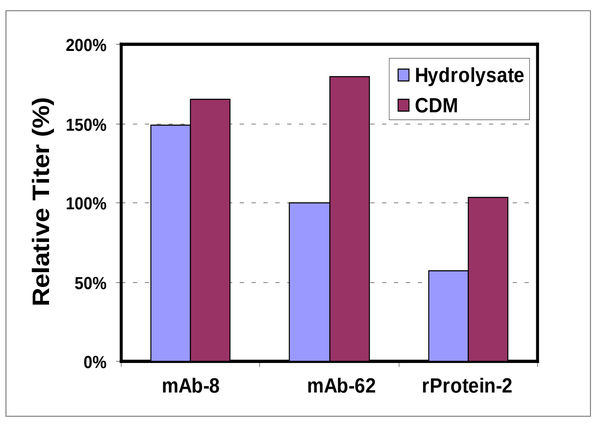


Employing a controlled pH shift, supports robust process upon scale-up enabled:

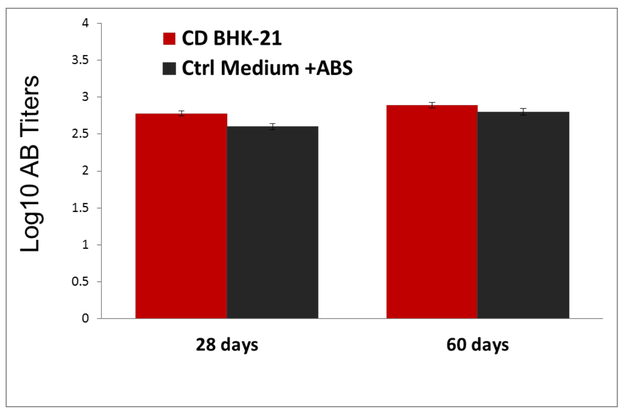
- **Consistent performance** from 5 -L to 250 – L Bioreactors.
- **50% titer improvement** over shake flask culture for a low producing clone.

Case Study 4: Reducing Process Variability and Supply Risk by Eliminating Complex Medium Components

Protein Production in CHO Cells



Virus Production in BHK-21 Cells



Switching platform medium and feeds from complex to chemically defined can maintain or even increase titers while:

- **Eliminating TSE/BSE concerns** by removing animal origin components
- **Reducing process variability** issues caused by inconsistency of complex components including serum and hydrolysates.
- **Reducing supply concern.**

CONCLUSIONS

The case studies discussed in this presentation highlight upstream development strategies that Thermo Fisher Scientific has used to help bioproduction customers:

- Increase productivity and product quality by optimizing feeds and feeding strategies.
- Improved process scale-up by optimizing pH control strategies.
- Improved process consistency by eliminating complex components.
- Reduced sourcing and supply risk by removing proteins and animal components from media and feeds.

MATERIALS

Case Study 1:
- CD CHO Medium with EfficientFeed B and EfficientFeed B+
- CD OptiCHO Medium with EfficientFeed A+

Case Study 2:
- CD CHO Medium with EfficientFeed B+ and GlycanTune B+ Total Feed

Case Study 3:
- Dynamis Medium with EfficientFeed C+

Case Study 4:
- Developed Medium and Feed
- CD BHK-21 Medium

Materials are for Research Use Only. Not for use in diagnostic procedures

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