

Product Information

CHO Feed Bioreactor Supplement

Without L-Glutamine or Glucose

Product Code C 1615

Storage Temperature 2-8 °C

Product Description

The expression of recombinant proteins is becoming increasingly important in academic research and the pharmaceutical industry. Chinese Hamster Ovary (CHO) cells are frequently used to express recombinant proteins, especially those proteins that require post-translational modifications for proper function.

Optimizing the cultivation of CHO cells in bioreactors is dependent upon the effectiveness of the culture processes. Fed-batch processes typically provide a more efficient supply of nutrients and allow for extended culture time when compared to batch culture processes. In fed-batch cultures, proper bioreactor supplements for feeding are critical.

CHO Feed Bioreactor Supplement is an animal component-free concentrated supplement developed specifically for fed-batch CHO cultures. This product is designed to replenish utilized nutrients such as amino acids and vitamins without significantly affecting the pH and osmolality of the culture. Using CHO Feed Bioreactor Supplement extends the length of culture, improves maximum cell density and increases recombinant protein productivity.

Intended Use

Caution: For manufacturing, processing or repacking.

Components

The formulation includes amino acids, vitamins, recombinant human insulin, plant hydrolysates, trace elements and other organic compounds.

This product does not contain glucose, L-glutamine, phenol red, antibiotics, antimycotics, or transferrin. This product does not contain hypoxanthine or thymidine, permitting its use with the dihydrofolate reductase (dhfr) gene amplification system.

Preparation Instructions

This supplement is supplied ready to use as a sterile liquid concentrate.

Storage/Stability

This product is stable when stored 2-8 °C and protected from light, until the indicated expiration date on the label.

Procedure

Aseptically add CHO Feed Bioreactor Supplement to the bioreactor system at the desired volume and frequency. Supplementation amounts and frequency can vary due to the differing nutritional requirements of specific clones, but 5ml CHO Feed Bioreactor Supplement per liter of reactor volume per day gives consistent positive results. Supplementing 10ml/L every other day as well as 2.5 ml/L every 12 hours also shows beneficial effects.

CHO Feed Bioreactor Supplement does not contain L-glutamine or glucose. Therefore, L-Glutamine (Product Code: G 7513) and Glucose (Product Code: G 8769) should also be added to your cultures, with the amounts and frequency dependent on the needs of your specific CHO clone.

Product Profile

To demonstrate the performance of CHO Feed Bioreactor Supplement, experiments were conducted using CHO cells cultured in suspension in Sigma-Aldrich CHO DHFR- Medium, Animal Component-free (Product Code C 8862).

For these studies, cells were inoculated at 5×10^4 viable cells/ml in 5-liter stirred bioreactors (Biostat® B, B.Braun International) at 5-liter working volume. The bioreactors were equipped with marine vortexing impellers and were instrumented for temperature, pH, dissolved oxygen and agitation control using digital control units. During all cultures, temperature was maintained at 37°C. The pH of the cultures was controlled at 7.1 through additions of CO₂ and Sigma's Bioreactor pH Adjustment Solution (Product Code B1185). Impeller speed was set at 70 rpm.

Supplementation with glucose, glutamine and CHO Feed Bioreactor Supplement began on day 4 of each culture. During all cultures, glucose levels were maintained at 4 g/L and glutamine levels were maintained at 4 mM. CHO Feed Bioreactor Supplement was added to fed-batch bioreactor cultures of a recombinant IgG producing CHO line at 5ml/L per day. The cultures that were supplemented with CHO Feed Bioreactor Supplement, glucose and glutamine were compared to batch cultures and fed-batch bioreactor cultures supplemented with only glucose and glutamine for growth, length of culture and productivity.

Figure 1 illustrates the comparison of cell growth amongst a batch culture, a fed-batch culture supplemented with glucose and glutamine, and two fed-batch cultures supplemented with CHO Feed Bioreactor Supplement, glucose and glutamine. All experiments used CHO DHFR Medium (C 8862) as the basal culture medium. CHO Feed Bioreactor Supplement consistently supported the highest viable cell density and length of culture.

Figure 1. Cell Growth Comparison

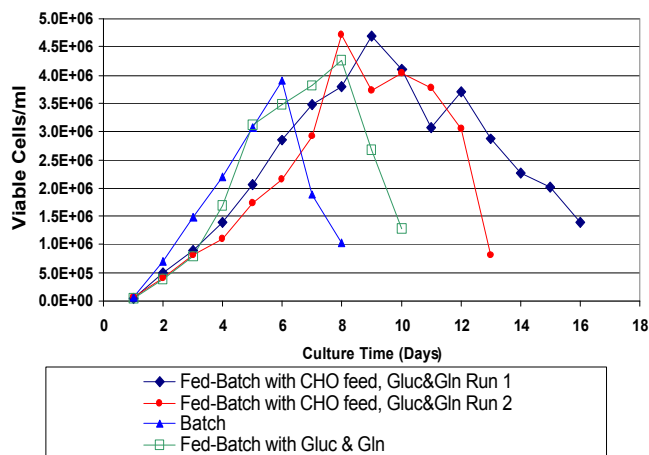
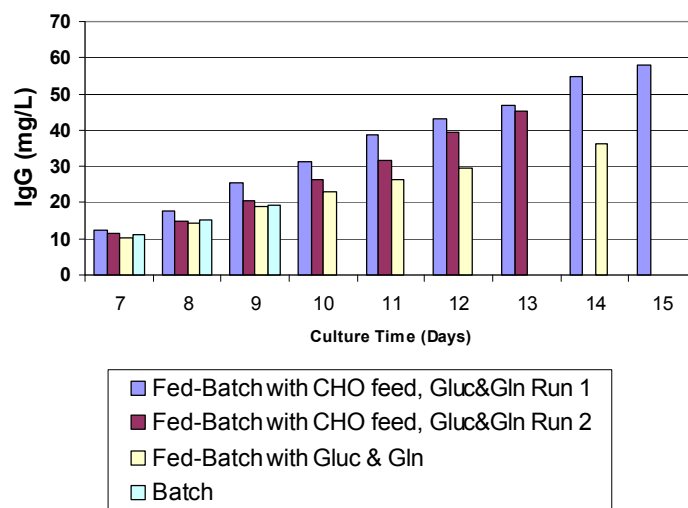


Figure 2 demonstrates that CHO Feed Bioreactor Supplement enhances IgG production compared to batch and fed-batch cultures supplemented with glucose and glutamine.

Figure 2. Productivity Comparison



References

1. Merten, O.W., Safety issues of animal products used in serum-free media. *Dev. Biol. Stand.*, **99**,167-180 (1999).
2. Mahadevan, Bioreactor Process Selection for Large Scale Manufacture of Monoclonal Antibodies-Tradeoffs and Recommendations. *Bioprocessing Journal*. May/June (2003).
3. Bjare, U., Serum-free culture. *Pharmacol. Ther.*, **53**(3), 355-374 (1992).

Precautions and Disclaimer

MSDS is available upon request or at www.sigma-aldrich.com.

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