

## Thermo Scientific HyClone Process Supplements Maximize Cell Culture Production and Performance



Developed through Metabolic Pathway Design™  
to Promote Maximum Cell Growth and Productivity

## Thermo Scientific Process Supplement Platform

The fed-batch version of stirred-tank culture has become most popular at large scales. The primary driver of this trend is based on adding nutrients to a batch culture in mid-run to increase the quantity of product harvested. The prevalence of fed-batch over other modes is due to many practical factors such as, reliability, ease of scalability and application latitude. In addition, one of the greatest improvements is derived from increases in the integral of viable cell concentration and volumetric productivity.<sup>1</sup>

Primary factors determining optimum feeding of cultures include:

- Preventing toxicity to initial low-density seed cultures
- Maintaining desired metabolic pathways in high-density cultures
- Prolonging cell viability and preventing induction of apoptosis
- Promoting longevity of cultures over short-lived peak densities
- Promoting high-quality product accumulation rather than mere quantity
- Encouraging product accumulation rather than simple culture biomass

Today's experienced fed-batch bioreactor operators can expect more than 10 times the efficiencies possible from a few years ago. Yields, for some secreted recombinant protein biologicals, are now expected to be 1-3 g/L of culture, with 5-10 g/L potentially achievable. As the newest research is applied to production scale, yields exceeding 10 g/L are anticipated.<sup>1</sup>

We have developed a Process Supplements platform to support demand in the area of fed-batch cell culture. Each supplement is developed through the Metabolic Pathway Design™ approach to provide specific nutrient combinations for a variety of applications, and have been successfully tested in CHO, hybridoma, NS0, HEK 293, PER.C6® (Crucell NV) and other cell lines.

The six Cell Boost supplements have been designed to provide such nutrients as amino acids, vitamins, lipids, cholesterol, glucose and/or growth factors in novel combinations for multiple mammalian cell types. HyClone Cell Boost supplements are chemically-defined and contain no animal derived components. In addition to the Cell Boost line, we offer concentrated liquid supplements designed to provide lipids and cholesterol to such cell lines as NS0, as well as specific nutrients for those cells using the glutamine synthetase (GS) Gene Expression System.



Each product in the Process Supplements platform has been rigorously tested in a variety of culture systems, including shaker flask cultures, traditional stirred-tank bioreactor cultures and disposable cell culture systems (e.g., the Thermo Scientific HyClone Single-Use Bioreactor). Utilizing various serum-free media formulations, the products on the Process Supplements platform have successfully improved cell productivity in some cases more than 10 times what is currently achieved.

<sup>1</sup>Whitford, W. Fed-Batch mammalian Cell Culture in BioProduction. BioProcess Intl. 4(4):30-44 (April 2006)



HyClone Single-Use Bioreactor (S.U.B.) 1000 L

## Thermo Scientific HyClone Serum-Free Media

To improve cell culture consistency and improve performance, applications for Serum-Free Media (SFM) can be found in many biotechnology applications including the production of recombinant proteins, monoclonal antibodies, viral vectors for gene therapy, and viral vaccines from mammalian and insect cell culture systems. As these applications scale-up to support clinical trials or manufacturing, the interaction between the serum-free medium and fed-batch process sup-

plements will be critical to achieving the highest level of cell productivity.

Thermo Scientific HyClone SFM is developed through the Metabolic Pathway Design™ approach to support superior performance in multiple cell culture platforms. This development process produces serum-free media targeted to increasing process yields for hybridoma, NS0, insect, CHO, HEK 293, MDCK, Vero and other cell lines. This has led to the

development of such state-of-the-art chemically-defined media as HyClone CDM4MAb™, HyClone CDM4PERMAb™, HyClone CDM4CHO™ and HyClone CDM4NS0™. These media provide the highest level of productivity and scalability while eliminating undefined and animal origin components. Each Thermo Scientific HyClone SFM has been successfully tested in a variety of cell culture systems including fed-batch bioreactors.

## Thermo Scientific HyClone Cell Boost 1™ (R05.2)

HyClone Cell Boost 1 is a supplement designed to provide nutrients such as amino acids, vitamins and glucose. It is designed to improve productivity through a multi-vitamin feed approach. HyClone Cell Boost 1 has been tested on a variety of cell lines including CHO and HEK 293 cells.

### Specifications

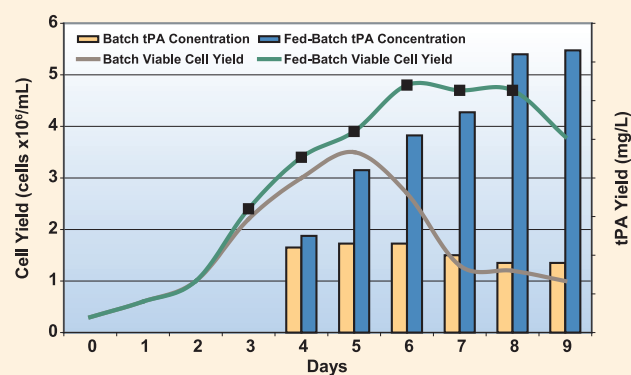
Chemically-Defined

Protein-Free

Animal Derived Component Free

Does not contain: L-glutamine & Pluronic® F68

HyClone CDM4CHO and HyClone Cell Boost 1 Culture



Production of recombinant tPA using a CHO cell line cultured in HyClone CDM4CHO™ during a 3 L stirred tank bioreactor culture. Fed-batch culture employed on days 3 through 8 using HyClone Cell Boost 1 (R05.2).

## Thermo Scientific HyClone Cell Boost 2™ (R15.4)

HyClone Cell Boost 2 is a supplement designed to provide nutrients such as amino acids and glucose. It is also designed to improve productivity through a single-vitamin feed approach. HyClone Cell Boost 2 has been tested on a variety of cell lines including CHO and PER.C6®.

### Specifications

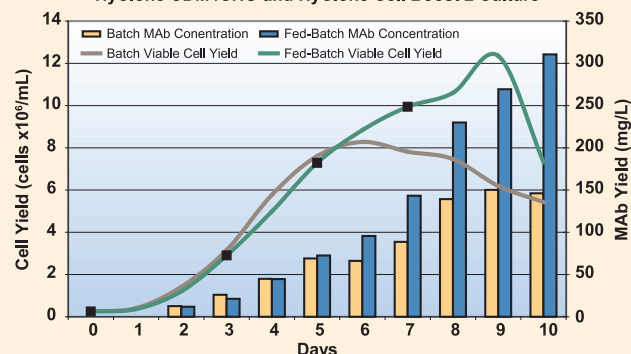
Chemically-Defined

Protein-Free

Animal Derived Component Free

Does not contain: L-glutamine & Pluronic® F68

HyClone CDM4CHO and HyClone Cell Boost 2 Culture



Production of Monoclonal Antibody using a rMAb CHO cell line cultured in HyClone CDM4CHO™ during a 3 L stirred tank bioreactor culture. Fed-batch culture employed on days 0, 3, 5 and 7 using HyClone Cell Boost 2 (R15.4).

## Thermo Scientific HyClone Cell Boost 3™ (JM3.5)

HyClone Cell Boost 3 is a supplement designed to provide nutrients such as glucose, amino acids, vitamins and trace elements. HyClone Cell Boost 3 has been tested on a variety of cell lines including, hybridomas and myelomas.

### Specifications

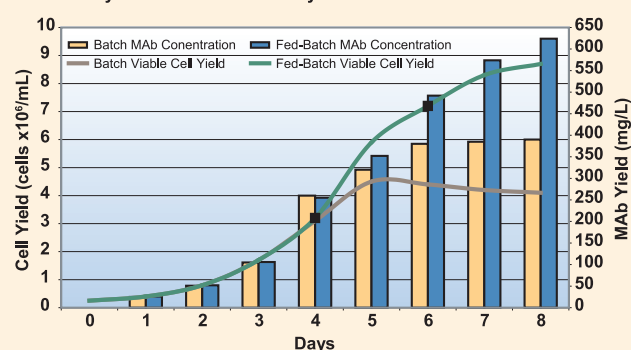
Chemically-Defined

Protein-Free

Animal Derived Component Free

Does not contain: L-glutamine & Pluronic® F68

HyClone CDM4MAb and HyClone Cell Boost 3 Culture



Production of IgG1 using a proprietary Sp2/0-derived hybridoma cultured in HyClone CDM4MAb™. Fed-batch culture employed on days 4 and 6 using HyClone Cell Boost 3 (JM3.5).

## Thermo Scientific HyClone Cell Boost 4™ (PS307)

HyClone Cell Boost 4 is a supplement designed to provide nutrients such as amino acids, vitamins, glucose, trace elements and growth factors. HyClone Cell Boost 4 has been tested on a variety of cell lines including CHO.

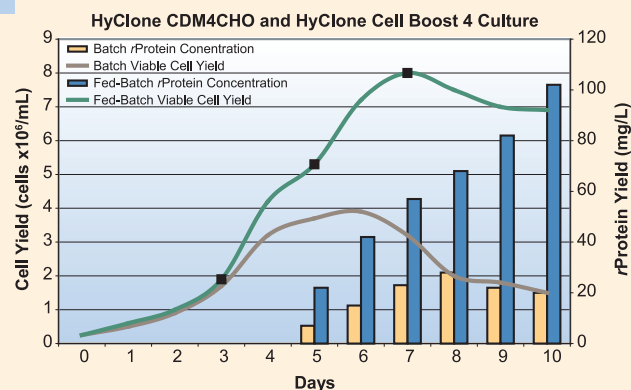
### Specifications

Chemically-Defined

Protein-Free

Animal Derived Component Free

Does not contain: L-glutamine & Pluronic® F68



Production of rProtein using CHO cell line cultured in HyClone CDM4CHO™ during a 3 L stirred-tank bioreactor culture. Fed-Batch culture employed on days 3, 5 and 7 using HyClone Cell Boost 4 (PS307).

## Thermo Scientific HyClone Cell Boost 5™ (CN-F)

HyClone Cell Boost 5 is a supplement designed to provide nutrients such as lipids, amino acids, vitamins and growth factors. HyClone Cell Boost 5 has been tested in a variety of cell lines including, CHO, Hybridoma, NS0 and HEK 293.

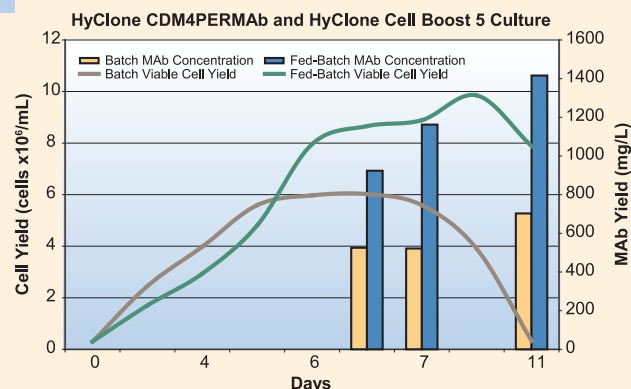
### Specifications

Chemically-Defined

Protein-Free

Animal Derived Component Free

Does not contain: L-glutamine & Pluronic® F68



Production of CD46 antibody in PER.C6® (Crucell NV) cells cultured in HyClone CDM4PERMAb™. Fed-batch culture employed daily feedings of HyClone Cell Boost 5 (CN-F).

## Thermo Scientific HyClone Cell Boost 6™ (CN-T)

HyClone Cell Boost 6 is a supplement designed to provide nutrients such as lipids, amino acids, vitamins and growth factors. HyClone Cell Boost 6 has been tested in a variety of cell lines including, CHO, Hybridoma, NS0, HEK 293 and T-cells.

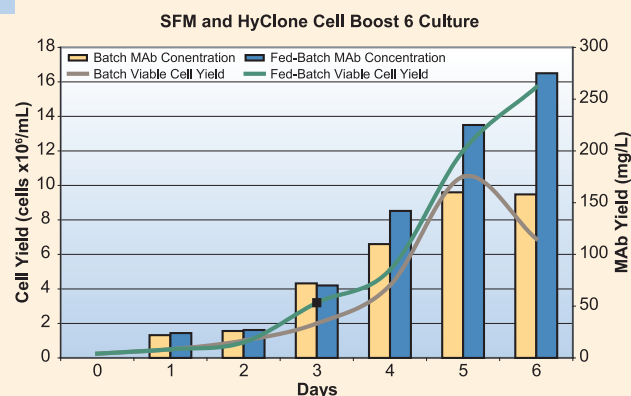
### Specifications

Chemically-Defined

Protein-Free

Animal Derived Component Free

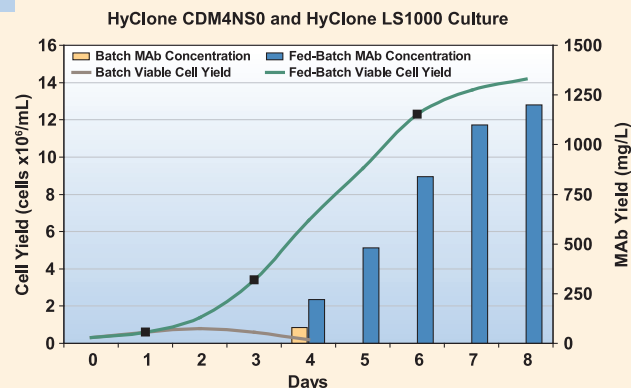
Does not contain: L-glutamine & Pluronic® F68



Production of IgG1 using a proprietary Sp2/0-derived hybridoma cultured in a serum-free media. Fed-batch culture employed on day 3 using HyClone Cell Boost 6 (CN-T).

## Thermo Scientific HyClone LS1000™

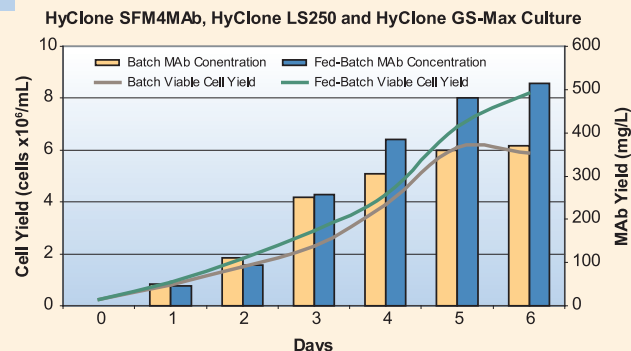
HyClone LS1000 is a chemically-defined, animal derived component free cholesterol supplement designed to be added as a fed-batch supplement. This 1000X concentrated supplement has been formulated using a proprietary complexing process for enhanced cholesterol delivery. It has been successfully tested in a variety of serum-free media cultures, including HyClone CDM4NS0™ and HyClone CDM4MAb™.



Production of Monoclonal Antibody using a proprietary NS0 cell line cultured in HyClone CDM4NS0™ during a 50 L Single Use Bioreactor culture. Fed-Batch culture employed on days 1, 3 and 6 using HyClone LS1000™ to overcome traditional cholesterol adsorption challenges in disposable cult culture systems with cholesterol auxotrophic cell lines.

## Thermo Scientific HyClone LS250™

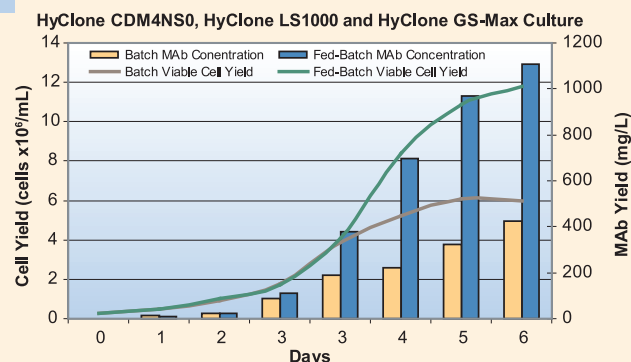
HyClone LS250 is a chemically-defined, animal derived component free lipid supplement developed to stimulate cell growth and MAb production in NS0 cell cultures using traditional hybridoma serum-free media. It has been successfully tested in a variety of media, including HyClone CDM4MAb™ and HyClone SFM4MAb™.



Production of MAb using a proprietary GS-NS0 cell line cultured in HyClone SFM4MAb™ with HyClone GS-Max™ supplement. HyClone LS250™ was added to both cultures to stimulate productivity. HyClone LS1000™ was added to the fed-batch culture as a 1000X concentrate beginning at 48 hours.

## Thermo Scientific HyClone GS-Max™

HyClone GS-Max is a chemically-defined, animal derived component free glutamine synthetase (GS) Gene Expression System cell culture supplement. Its development has built upon traditional GS supplement formulations to provide the additional nutrients needed for high productivity in GS-cloned CHO and NS0 cell lines. It has been successfully tested as both a media preparation supplement, and as a fed-batch supplement.



Production of IgG using a proprietary GS-NS0 cell line cultured in HyClone CDM4NS0™ during 100 mL shaker flask cultures. Fed-Batch culture employed HyClone LS1000™ and HyClone GS-Max™ at 72 hours.

## Ordering Information

### Thermo Scientific HyClone Cell Boost™ Process Supplement Kit (SH30890)

The HyClone Cell Boost Process Supplements Kit contains 6 x 100 g samples of supplements designed to increase cell productivity in a variety of cell lines. Each supplement is designed to provide nutrients to fed-batch culture applications. The supplements are chemically-defined and contain no animal components. They have been tested in a variety of cell culture systems, including shaker flasks and bioreactors. Each supplement is available in larger packaging configurations.

| Product Name         | Amino Acids | Vitamins | Glucose | Trace Element | Growth Factor(s) | Lipids | Cholesterol |
|----------------------|-------------|----------|---------|---------------|------------------|--------|-------------|
| Cell Boost 1 (R05.2) | ✓           | ✓        | ✓       |               |                  |        |             |
| Cell Boost 2 (R15.4) | ✓           | ✓        | ✓       |               |                  |        |             |
| Cell Boost 3 (JM3.5) | ✓           | ✓        | ✓       | ✓             |                  |        |             |
| Cell Boost 4 (PS307) | ✓           | ✓        | ✓       | ✓             | ✓                |        |             |
| Cell Boost 5 (CN-F)  | ✓           | ✓        | ✓       | ✓             | ✓                | ✓      | ✓           |
| Cell Boost 6 (CN-T)  | ✓           | ✓        | ✓       | ✓             | ✓                | ✓      | ✓           |

| Liquid Supplements                | Part #  | 50 mL | 100 mL | 500 mL | 1000 mL |
|-----------------------------------|---------|-------|--------|--------|---------|
| LS250                             | SH30555 |       | ●      | ○      | ○       |
| LS1000                            | SH30554 | ○     | ●      | ○      | ○       |
| GS-Max                            | SH30586 |       | ○      | ○      | ○       |
| Powder Supplements                | Part #  | 100 g | 500 g  | 1000 g | 5000 g  |
| Cell Boost 1 (R05.2)              | SH30584 | ●     | ●      | ●      | ●       |
| Cell Boost 2 (R15.4)              | SH30596 | ●     | ●      | ●      | ●       |
| Cell Boost 3 (JM3.5)              | SH30825 | ●     | ●      | ●      | ●       |
| Cell Boost 4 (PS307)              | SH30857 | ●     | ●      | ●      | ●       |
| Cell Boost 5 (CN-F)               | SH30865 | ●     | ●      | ●      | ●       |
| Cell Boost 6 (CN-T)               | SH30866 | ●     | ●      | ●      | ●       |
| Cell Boost Process Supplement Kit | SH30890 |       |        |        |         |
| Cell Boost 1 (R05.2)              |         | ●     |        |        |         |
| Cell Boost 2 (R15.4)              |         | ●     |        |        |         |
| Cell Boost 3 (JM3.5)              |         | ●     |        |        |         |
| Cell Boost 4 (PS307)              |         | ●     |        |        |         |
| Cell Boost 5 (CN-F)               |         | ●     |        |        |         |
| Cell Boost 6 (CN-T)               |         | ●     |        |        |         |

● Item in stock; ○ Item is made to order. Lead times and minimum order quantities apply.

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