



CDM-HD SERUM REPLACEMENT

Chemically Defined Medium for High Density Cell Culture

- Use like Serum
- Chemically Defined
- Protein Free
- Purification Simplified

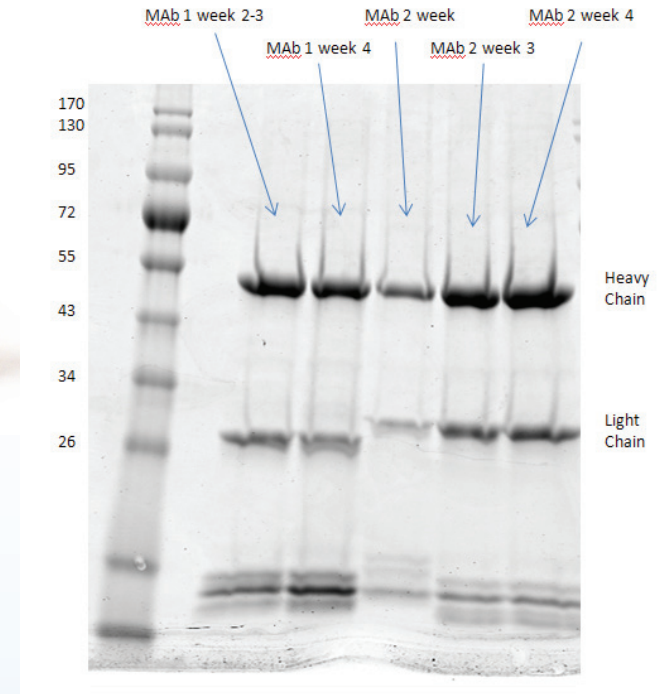
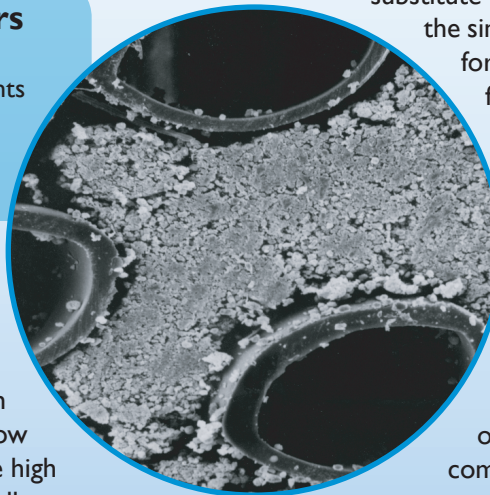


CDM-HD Serum Replacement is a chemically defined, protein free serum replacement that permits any basal medium such as DMEM or RPMI to be used without serum. CDM-HD is designed specifically for the culture of cells at high density and optimized for use in FiberCell® Systems hollow fiber bioreactors. Secreted products such as monoclonal antibodies and recombinant proteins are free of contaminating proteins from the medium and can be purified using simplified protocols, increasing net yield in many cases. CDM-HD provides lot-to-lot consistency and is an economical replacement for serum. It is available as a dry powder to make up one liter and is used at a concentration of 10%. The cost of CDM-HD is less than serum giving you all the benefits of a chemically defined,

Optimized For Hollow Fiber Bioreactors

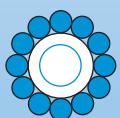
- Composition balanced for high-density culture.
- No detergents or other cell membrane stabilizing agents that sometimes interfere with assays or precipitations
- Increased buffering capacity maintains optimum conditions for protein and antibody production.

protein free medium without the high price. Hollow fiber cell culture is an ideal method for the production and collection of secreted products from mammalian cells. A large numbers of cells be supported in a small space and the secreted product is concentrated to a high degree. The high surface area to volume ratio of hollow fiber bioreactors (100cm²/ml or more) and the extreme high flux rates of fibers from FiberCell® Systems allows cells to grow at 100X the density found in flask culture (10⁸ vs. 10⁶/ml). It is one of the only cell culture methods that permits cell densities similar to those found *in vivo*. High cell density



allows cells to be grown in reduced serum environments (as low as 2% vs. 10% for conventional culture methods) and more easily adapted to commercially available serum free mediums. However, these mediums can be expensive and sometimes optimal for only a limited number of cell types. The concept of CDM-HD is simple: provide a universal serum substitute that can take advantage of the simplified serum requirements for cells grown in hollow fiber bioreactor systems. CDM-HD represents a true breakthrough in cell culture ideology and technology. It is the first time that a culture medium takes advantage of the specific growth of cells at a high density in order to simplify and optimize that medium's composition.

ABOVE: Cross-section of hollow fibers in FiberCell® Systems hollow fiber bioreactor. High-density cell growth is shown in extracapillary space.



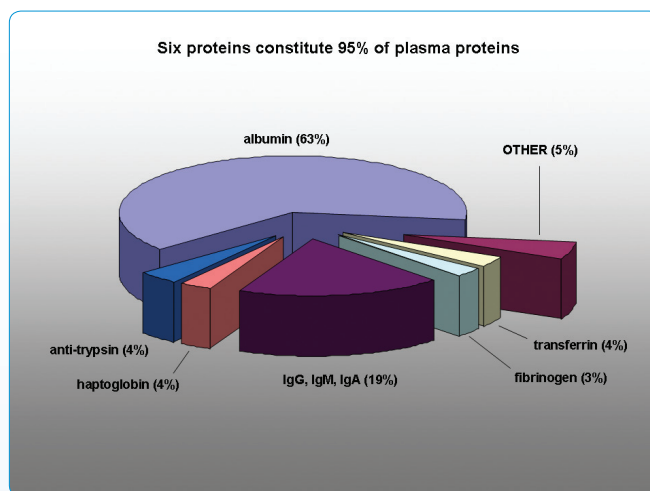
FiberCell Systems Inc.
a better way to grow cells

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SERUM	CDM-HD
High degree of lot-to-lot variability	No variability
High protein content	Animal-derived component free
Purification can be difficult	No extraneous protein to complicate purification
Price fluctuates	Price stability
Advantageous virus contaminants	No viral contamination
Regulatory unfriendly	Regulatory friendly

culture derived products. Serum proteins must be removed during purification. A totally defined, animal component free, protein free medium will not contain any proteins nor any materials derived from animals and will have high lot-to-lot consistency. Purification of the desired secreted product is facilitated and regulatory compliance is made much simpler.

BELOW: Various components of serum. The major component, BSA binds many substances non-specifically and can be an overwhelming protein burden in some purification schemes, immunoglobulins can interfere with specific antibody purifications and the "other" can have many undefined effects. None of these characteristics will be reproducible from lot to lot.



The beneficial effects of serum supplementation are offset by several disadvantages: serum is an ill-defined mixture and often contains adventitious agents and by-products like bacterial endotoxins and other immunogenic contaminants. Furthermore, batch qualities vary and the costs can be high. Sera are a major source of viral contaminants that often do not produce cytopathic effects or morphological changes but once present are almost impossible to remove from cultures. Some important advantages in the use of totally defined media are the avoidance of risks of contamination and immunogenic stimuli and lot-to-lot consistency. Possible contaminants include viruses, prions and mycoplasma which highly impair pharmacologic use of

INSTRUCTIONS FOR USE: Reconstitute the contents of one bottle of CDM-HD in distilled water to make a total volume of 1 liter. Adjust pH to no higher than 6.5 using 1N NaOH. Sterile filter, do not autoclave. Add to any basal medium at a concentration of 10%. When using with FiberCell® Systems hollow fiber bioreactors add 10% FBS to the cell inoculum when loading cells to provide attachment factors. No adaptation is required though you may see a reduction in glucose uptake rate for the first day or two of use. CDM-HD is stable for at least 1 month as a concentrate when stored at 4 degrees and away from light.

NOTES:

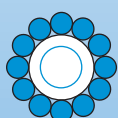
- CDM-HD will not require any adaptation but is optimized for cells growing at high density. For best results switch to CDM-HD after cells have reached a high density inside the FiberCell® Systems hollow fiber bioreactor, typically after one week of culture or so.
- CDM-HD contains 1 gram per liter glucose at 10%. When working with a low glucose medium such as RPMI it is important to monitor the glucose concentration closely.
- CDM-HD is protein free and does not contain any cell attachment factors. When inoculating cells in medium containing CDM-HD add 10% FBS to the cell inoculum only. This will provide the required attachment factors for adherent cells. This is not required for suspension cells though hybridoma cell lines should be treated as adherent cells.
- CDM-HD can be used in other culture systems such as spinner culture and roller culture. For these applications add a surfactant such as pluronic F68 or some other cell membrane protecting surfactant.
- CDM-HD is protein free. The secreted protein of interest may be the only significant protein present in your cell culture supernatant. You should re-evaluate your purification protocols as entire steps can sometimes be eliminated, increasing yield. Keep in mind that CDM-HD is protein free and contains no ferritin so the free iron levels will be higher than in standard mediums. Pay attention to any chelating agents that may be part of your buffers or purification protocol.

For technical support contact FiberCell® Systems.

Product Ordering ID: CDM-HD-I

Powder to make 1 Liter

Proteomics Analysis of Nasopharyngeal Carcinoma Cell Secretome Using a Hollow Fiber Culture System and Mass Spectrometry Hsin-Yi Wu, Ying-Hwa Chang, Yu-Chen Chang, and Pao-Chi Liao J. Proteome Res., 2009, 8 (1), 380-389 DOI: 10.1021/pr8006733



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