

Cell & tissue culture media

Instrumentation through innovation

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SPECIAL POINTS OF INTEREST:

Major companies working in cell culture media

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- Animal free media
- A possible re-search direction

A bio-technology news letter

It is often said that media is one of the most important parameters. Major companies working in this direction are

- *Shawn Smith of In Vitrogen. Gibco cell culture systems,*
- *Prof Florian Wurm of Swiss Federal institute of technology*
- *Cheristian Simonsen of Sierra Bio-Sources*
- *Sigma- Aldrich a company setting up a 25 Scientist Research facility on culture media,*
- *Chuck Velnoskey of BD www.bd.com*
- *Sandra Parten at Irvine Scientific*
- *Dr. Etch berger of JRH Bio sciences*
- *Ferruccious Messi of cell culture Technologies*
- *Frenz Schulte of Biochrom*
- *Lance Mikus product manager of Bio-Source*
- *Brandon Pence (www.hyclone.com)*
- *IRVINES rational culture media design. TM*

All believe and work for the development of the so-called wonder formulation of cell culture media. So far serum based formulation are used as culture media where as safety consideration and regulations are forcing the manufactures to go for animal free media components. Cell culture medium is generally accepted by one and all as the most important criteria for cell culture productivity. More than 50 amino acids, sugars, ions, vitamins, lipids and other ingredients form a typical culture medium.

However the wonder composition which can provide four to five cell doublings is still

eluding various research groups and is the hottest topic for industrial research.

Eventually media development will employ easily measured, short time course culture events that correlate to high productivity and growth. It is important to industry to have a reportable event activity that signals absolute growth rather than growth rate.

Cells that double every 18 Hrs may not be better than that double every 24 Hrs. since the first variety may have only two to three doubling where as the second or slower cells may provide five or more generations. So for no explanation or scientific reasoning is available as to why some cell grow faster and some others multiply more no of times.

The trend towards animal free manufacturing ingredients has hindered media development. New media (animal-free) while eliminating real health risk have introduced regulatory uncertainty. Also animal protein free media are phenomenally expensive since they replace cheap bovine serum components with pharmaceutical grade reagents. So far no real substitute is found for Bovine Serum Albumin, that preserves and protects proteins. Recombinant 'BSA' costs about ten times as much as natural material.

End users, that is mostly large pharmaceutical contract manufactures have a much greater appreciation of the impact of media and the overall bioprocess systems performance on the final cost

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of the product. The growth optimal productivity and regulatory compliance are the primary focus behind choices of media. In Europe large contract manufacturers are buying cru cell's proprietary 'Per C6' cell line.

Most serum free media still use-undefined components like plant protein hydrolysates generated from the action of digestive enzymes on vegetable proteins to obtain di and tri-peptides. Some of these materials in this digest are nutritional but a few are meant for regulatory and or carrier function. No one is really sure about the specific fractions role in the digest.

Media vendors took the idea of defined media a step further and replaced the protein hydrolysate by chemically defined peptide ingredients.

The chemically defined media are more consistent, though somewhat lower in performance. Until defined media formulations work as good as serum free formulations manufacturers will give up 100% consistency for higher productivity Sigma- Aldrich the leading supplier of reagents and fine chemicals pushed the idea of defined premixed and powdered media. Sigma offers media development kits, CHO optimizations kits 1 and 2 based on media mixing and experimental matrix techniques. They also provide a free 30-day free download of 'state ease expert'- a design of experiment software from website www.stateease.com

A refined, upgraded and optimized vegetable protein "hydrolysates", is being sold by BD (www.bd.com) as principal components of cell culture media. Hydrolysates from different sources are unique with respect to amino acid content. Defined media offers interesting possibilities for experimenting and the potential to create "super media" Chemically defined cell culture media avoids regulatory concerns associated with animal derived components while providing greater opportunity for process optimization.

Yet another company 'Hyclone' is developing serum free media using metabolic pathway design technology that balances nutrient supply against metabolic waste accumu-

lation. This approach determines the effective dose of nutrients critical to the production of recombinant biological and provide complex lipids and phospholipids that facilitate delivery through cell membrane to ensure optimal yield and productivity. Yet another development in the large and medium manufacturing process is going from "Batch Process to a continuous process" This implies addition of highly concentrated media consistently. In fact the demand is for multi compendia raw materials that are accepted by multiple pharmaceutical companies world over.

Cell culture technologies (www.cellculture.com) has developed a chemically defined, serum, protein and peptide free culture media since such minimal media, contain only chemically defined small molecule-based ingredients factors such as cell culture reducibility and results interpretation becomes more consistent.

Working with industry and research organizations worldwide to develop customized media for specific research needs "cell culture technologies" offer media kits and whole cell culture systems for the production of recombinant proteins, monoclonal antibodies and viral replication in standard human and animal cell lines. Dr.Ferruccio Messi CEO of "cell culture Technologies" is the person, who can provide more information in this regard.

The potential of Indian college and research Labs, having a large number of trained bioengineering personnel can be better employed. They can attend to and supervise a large experimental base to conduct studies and research in the field of 'appropriate media' and whole cell culture line systems. This results in cutting down cost of inputs into cell culture and drug research. Thus our ability potential, and personnel availability will give us lead in fine tuning the media in which the cells grow. India can, thus contribute in defining critical factors such as cell viability, product yield, purity optimizing drug discovery and development. If these goals are pursued diligently in five to ten years time India can become leader in Bio-research.

In our next issue:

Downstream processing (DSP)

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