MAM-PF®

CHO PRODUCTION MEDIA

Benefits at a glance:

- ACF (Animal Component Free)
- Chemically defined
- High cell densities
- Pharmaceutical application
- High product yield

BioConcept

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History

Forty years of experience serving the Swiss biological community.

2015 the brand new liquid media production plant was opend.

1993 BioConcept added the Amimed® brand to its portfolio.

BioConcept has developed a strong international presence with its Amimed® brand.

BioConcept has a positive reputation because the company is constantly updating its practices in order to keep up with the advancing field of cell biology.

Flexibility

BioConcept is a privately held company.

BioConcept listens to the customers' needs and does its utmost to meet them.

Powder and liquid media plants.

Batch sizes from 5 up to 5,000 Litres. 1 kg powder up to 800 kg.

Production with WFI (Water For Injection).

Media can be delivered within a few weeks if needed.

Facilities

In 2015 BioConcept opened its brand new liquid media plant. The plant was designed to uphold a maximum degree of sterility through its state of the art air processing system and advanced machinery.

More information:
www.bioconcept.ch/de/Downloads

Highlights

of the MAM-PF® series

Animal Component Free
MAM-PF® media do not contain proteins or undefined hydrolysates.

Chemically defined
BioConcept holds TSE certificates for each component to ensure EMA/410/01 conformity.

Easy adaptation
In many cases it is possible to switch directly from your current medium to MAM-PF®.

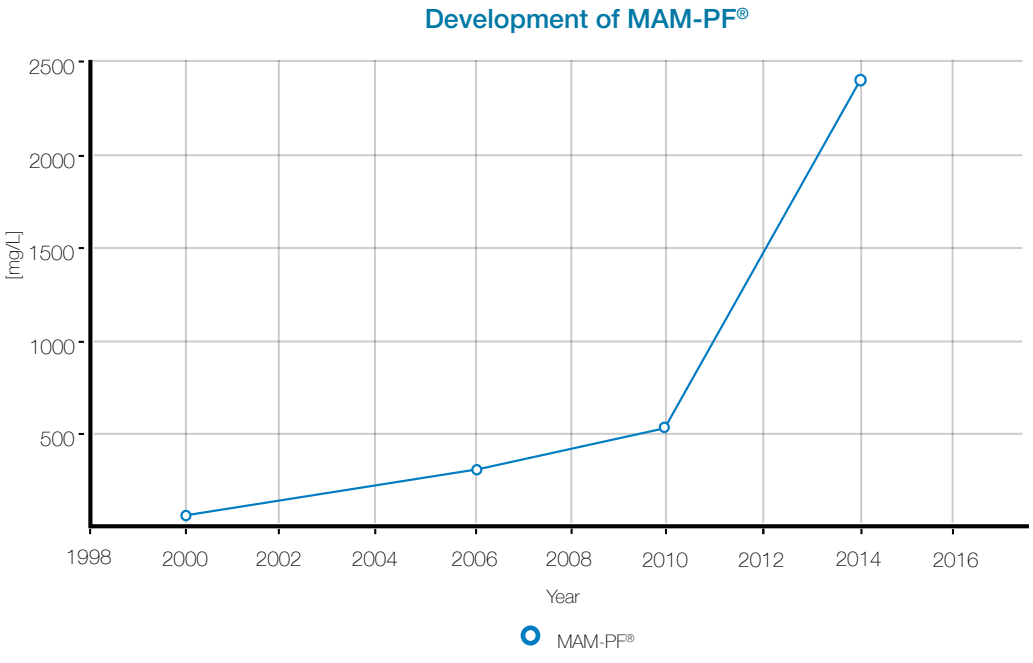
High cell density combined with high product yield
- Antibody production of up to 5.5 g/L.
- EPO of up to 2.5 g/L (see graph below).
- Cell density up to 3.7 x 10^7 cells/ml.

Liquid batch capacity
Batch sizes ranging from 5-5000 litre, water for injection (WFI) is the highest quality available.

Powder batch capacity
Batch sizes ranging from 1 - 800 kg, our milling process results in particle sizes of around 20 µm (d50). This leads to a quick dissolution of the powder medium.

Feed mixes
Various feed mixes are available for high density cell culture and high productivity.

Glycosylation
Best glycosylation pattern observed.



Increase of Erythropoietin (EPO) yields during the system development. Within the last 4 years the product yield could be quadrupled up to 2.3 g/L using the MAM-PF77® medium and FMS3 in a fed-batch.

MAM-PF® series

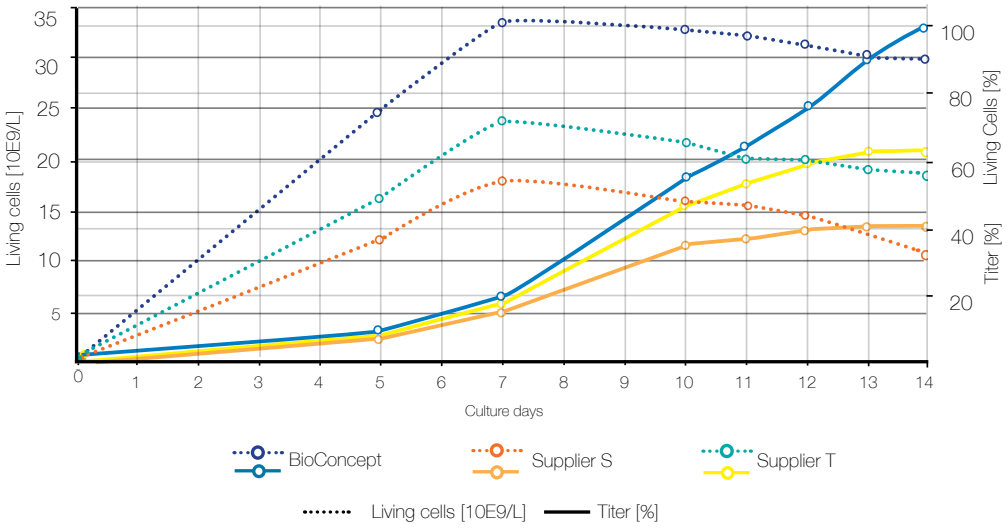
MAM-PF® (Mammalian Artificial Medium - Protein Free) media are Animal Component Free (ACF) and in accordance with the strict quality guidelines EMA/410/01. MAM-PF® is a production media. It is protein-free and protein hydrolysates free, chemically defined and for high cell density cultivation of a variety of cell lines such as CHO (Chinese Hamster Ovary) cells or BHK (Baby Hamster Kidney) cells and the high level expression of recombinant proteins. BioConcept holds a certificate for every single component used in the MAM-PF® media series to guarantee an untainted and exceptional final product.

Performance

Cell Density

CHOSI cells cultured in MAM-PF77® have shown the fastest growth and a ~100% and ~40% higher cell density compared to media by Suppliers S and T. This corresponds with the final product titers at the end of the fed-batch, respectively (All cultures were fed with FMS3 in the same feed regime). The higher viability in the stationary phase shows that the glycosylation in MAM-PF77® was superior.

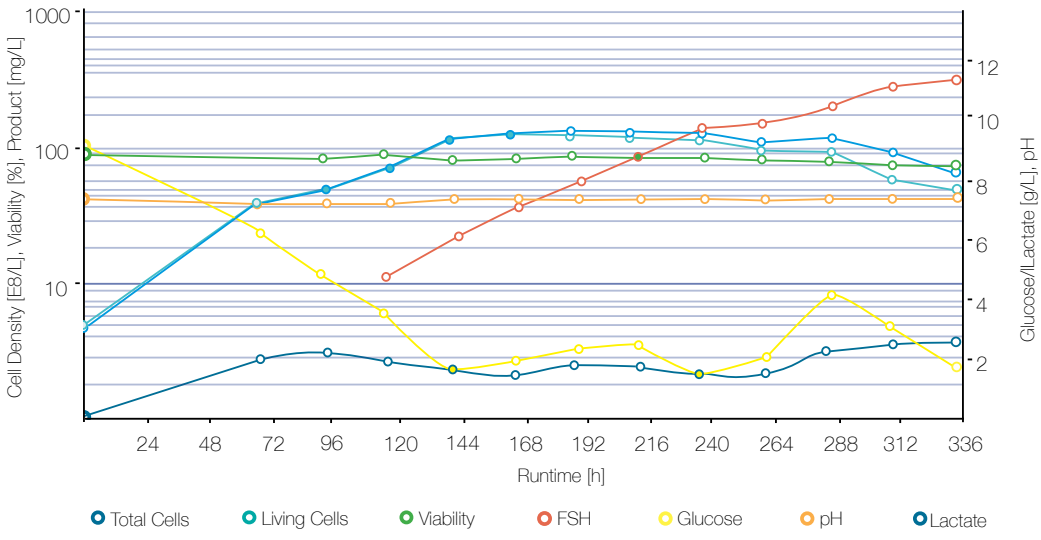
MAM-PF® and Other Suppliers



Performance of MAM-PF77® and two different CHO media suppliers in a 14-day fed-batch mAb production.

Application Data FSH

FSH produced with MAM-PF® and FMS3



14-day bioreactor production scheme of the high glycosylated follicle-stimulating hormone (FSH) using MAM-PF77® and the FMS3 feed mix.

FSH

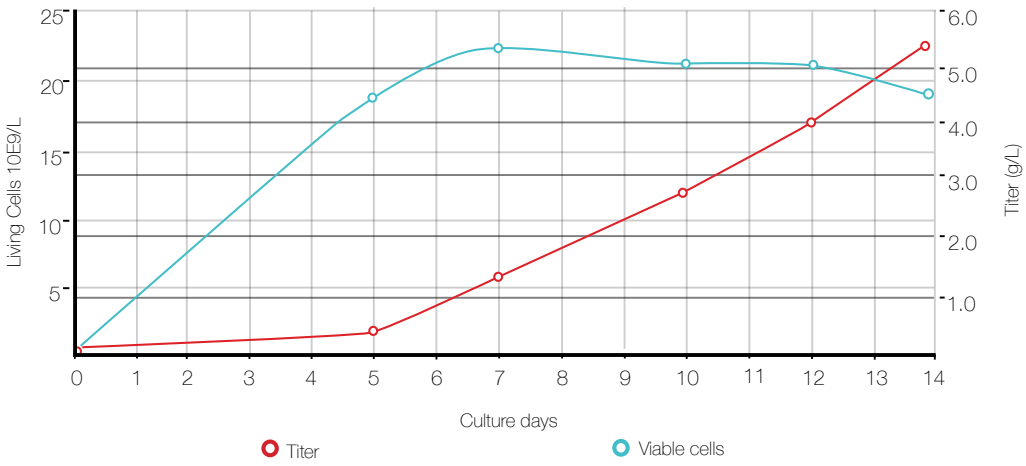
A cell density of over 100 mio. cells per liter can be reached through mixing the CHO feed mix FMS3 to MAM-PF77®. It is possible to achieve a titer of over 350 mg/L of the highly glycosylated follicle-stimulating hormone (FSH) within 14 days in a stirring bioreactor tank , making it a very high quality product. As determined during the purification process, 45% of the product showed an isoform-pattern, low aggregates, and low oxidized forms. MAM-PF77® can be used to produce quality FSH that fulfills its Ph.Eur. requirements.

Application Data Antibody

Ipilimumab

The continuous innovation and development of the MAM-PF® media series has lead to the brand new MAM-PF77® cell culture medium and CHO Feed Mixes FMS3 and FMU. MAM-PF® media now increase productivity of Ipilimumab (monoclonal antibody) by up to 5g/L. The new expression system is also viable in fed-batch and perfusion systems.

Ipilimumab produced with MAM-PF® and FSU



High yields of mAbs, e.g. > 5g/L Iplimumab can be reached in a 14-day fed-batch system using MAM-PF77® plus the novel CHO feed mix FMU.

Selection of pre-developed biosimilars produced with MAM-PF® media series.

API (Indication)	Available (EUGENEX Biotechnologies)	Brand Name (Orginator)	Global Sales 2012 Estimates [Mio $]
EPO, Epoetin alpha (Anemia)	Cell-Line & USP & DSP	**Epogen** (Amgen) **Eprex** (Johnson)	~5.000
DPO, Darbepoetin alpha (Anemia)	Cell-Line & USP & DSP	**Aranesp** (Amgen)	~2.500
INFb, Interferon beta 1a (MS)	Cell-Line & USP & DSP	**Avonex** (Biogen) Rebif (Serono)	~1.200
FSH, follicle stimulating hormon (Infertility); also hCG & LH	Cell-Line & USP & DSP	**Gonal-F** (Serono) Puregon (Organon)	~500 ~300
Etanercept, TNFa receptor IgG (chronical arthritis, psoriasis)	Cell Line USP & DSP	**Enbrel** (Amgen, Pfizer, Takeda)	~8.400
Adalimumab,TNFa Mab (rheumatoid arthritis, Crohn's)	Cell Line USP & DSP	**Humira** (Abbott)	~9.300
Rituximab, CD20 Mab (rheumatoid arthritis, lymphoma)	Cell Line USP & DSP	**Rituxan** (Roche)	~6.900
Trastuzumab, HER2 Mab (mammacarcinom)	Cell Line USP & DSP	**Herceptin** (Roche)	~6.100
Bevacizumab, VEGF Mab (colorectal cancer)	Cell Line USP & DSP	**Avastin** (Roche)	~6.300
Cetuximab, EGF receptor Mab (colorectal cancer)	Cell Line USP	**Erbitux** (BMS,Imclone)	~1.000
Omalizumab, IgE Mab (persistent allergic asthma)	Cell Line USP	**Xolair** (Genentech/Novartis)	~1.000
Denosumab, RANKL IgG (osteoporosis, colorectal cancer)	Cell Line USP	**Prolia** (Amgen)	~500
Eculizumab, Complement C5 Mab (hemoglobinuria (PNH))	Cell Line USP	**Soliris** (Alexion)	~1.100
Ipilimumab, CTLA-4 IgG1 (metastatic melanoma)	Cell Line USP	**Yervoy** (BMS)	~1.000
Tocilizumab, IL-6R IgG1 (Castelman, rheumatoid arthritis)	Cell Line	**Actemra** (Roche, Chugai)	~1.000
Abatacept, CTLA-4-IgG1 fusion (rheumatoid arthritis)	Cell Line	**Orencia** (BMS)	~1.000
Pertuzumab, Her2 dimer inhibitor (metastatic breast cancer)	Cell Line USP	**Omnitarg** (Roche)	~1.000
Panitumumab, EGF-R Mab (colorectal cancer)	Cell Line	**Vectibix** (Genentech/Novartis)	~ 400
Ofatumumab, CD20 IgG1 2nd Gen. (leukemia and others)	Cell Line	**Arzerra** (Genmab/GSK)	~100

Biosimilars and MAM-PF®

Biosimilars are highly diverse and complex. The medicines are a large group that include growth factors, cytokines, hormones, monoclonal antibodies (mAb) and, potentially, vaccines (Huzair and Kale, 2015). Due to their complexity and post-translational modifications (e.g. glycosylation of mAbs), many biosimilars are produced using the CHO (Chinese Hamster Ovary) expression system. Finding a medium that meets the strict regulations set for biosimilar production and creates a highly superior product can be challenging. Nevertheless, you must look no further: At BioConcept we offer high quality products that are both fully chemically defined and animal component free. This is the ground-breaking MAM-PF® media series. In the adjoining table you will find a selection of successfully produced biosimilars that are cultured with MAM-PF® media in the designed expression CHO host cell line (propriety of EUGENEX Biotechnologies).

Selection of references for the MAM-PF media series:

Harald Zähringer (2009). Product survey: Protein expression systems :New Protein Factories. Lab Times (6) 58-63.

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Link, J, Rattenholl, A., Lütkemeyer, D., and Gudermann, F.Characterisation of gas transfer properties in shake flasks using disposable pH and dissolved oxygen sensors and their application in mammalian high cell density cultures (Poster). URL: http://microsite.sartorius.com/fileadmin/Image_Archive/microsite/sensolux/pdf/11_05_12_Poster_Sensolux.pdf

Schumann et. al. (2009). Method for purifying erythropoietin. United States Patent No: US 7,619,073 B2.

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