presents

ChangeClear™

A paradigm shift in technology for cell culture clarification and purification!

QUICK	FLEXIBLE	REMOVES
Multiproduct Formats	High Cell Titer	Turbidity
Low Validation Costs	High Cell Viability	Endotoxins
Quick Product Change Over	Any Bioreactor Scale	HCP /Viruses
		DNA

A cost-effective single-use technology based on Celpure® powder technology!

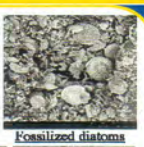
How to Apply Techniques to New Disposable Processes

Results were published on a poster presented by Merck Serono Biodevelopment, Martillac, France.

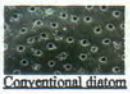
Introduction

Diatomaceous earth (*Baccillariophyta*)

- Silica skeleton of unicellular algae treated heat (above 1000°C), acid solutions, calcination.
- One of the components of depth filters used for cell removal and nanofilter prefiltration.
- Single Use and inexpensive technology.



Fossilized diatoms



Conventional diatom

Celpure®

Celpure®

- Highly purified diatomaceous earth with low endotoxin and low impurities level.
- GMP grade Diatomaceous earth.
- Can be directly provided in diposable bags.

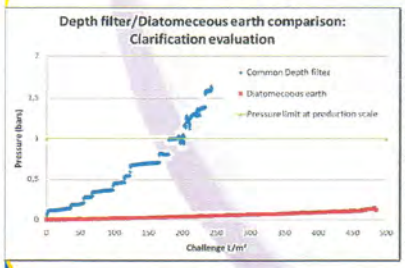
	Celpure® 300 (high purity grade)	Celite Standard Super-Cel® (conventional grade)
Al	nd* (PPB)	1840 (PPB)
Ca	nd	1050
Mg	124	1010
Fe	56	400
Zn	nd	210
Cu	12	16
Sb	nd	12
Mn	4	14
Cr	nd	4
Cd	nd	0.6

*(nd) Below detectable limit

Table comparing impurities level

Results

Use of Celpure® for clarification step

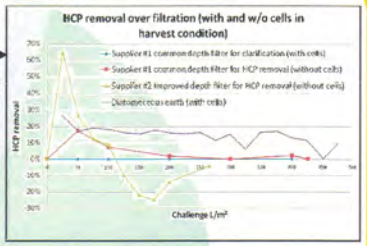


- Diatomaceous earth has at least 50% more filtrability capacity than classical depth filter.
- Cost is reduced by 2 fold by using Celpure® instead of depth filter.
- Use of slurry in disposable bag (ChangeClear) facilitates Celpure® handlings.

Use of Celpure® for host cell proteins removal

- HCP removal even with cells

Basic pI Protein	AEX	98%	52%	97 %
Acidic pI Protein	AEX	99%	67%	ND

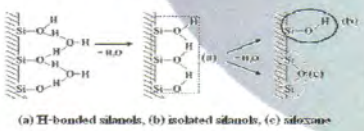


- HCP and DNA removal improved without cells

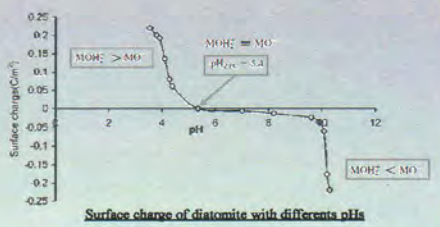
Discussion

Interactions with Celpure®

- Incompressible porous particles keep flow while retaining particles in the inner surface.
- Different silica forms depending on pH :
  - Ionic interactions (a), (b)
  - Hydrophobic interactions (c)



(a) H-bonded silanols, (b) isolated silanols, (c) siloxane



Surface charge of diatomite with differents pHs

- Celpure® could replace a chromatographic resin or a charged membrane (cost saving).

Conclusions

By improving cell growth and productivity, DSP is foreseen as the future bottleneck for biotechnology companies. Whereas some industries are investing more and more in costly new technologies, Merck Serono Biodevelopment has decided to explore other inexpensive, disposable and well-known techniques used in other industries. Diatomaceous earth is one of the components of single-use depth filters used in biotechnology companies for cell clarification, nanofilter prefiltration and recently, as some studies have shown, for removal of contaminants. Highly Purified diatomaceous earth (Celpure®), with low endotoxin and low impurity levels, is now available for GMP manufacturing purposes. Cell clarification studies demonstrated that Celpure® is 2 up to 3 fold more efficient than depth filters in removing cells and can replace centrifugation step. Besides a partial impurities removal was also obtained even with cells. Moreover, the first trials on clarified harvests demonstrated the ability of such technology to remove up to 67% of impurities in the filtrate. Celpure® can be used at different purification steps and even replace classical chromatographic resins.

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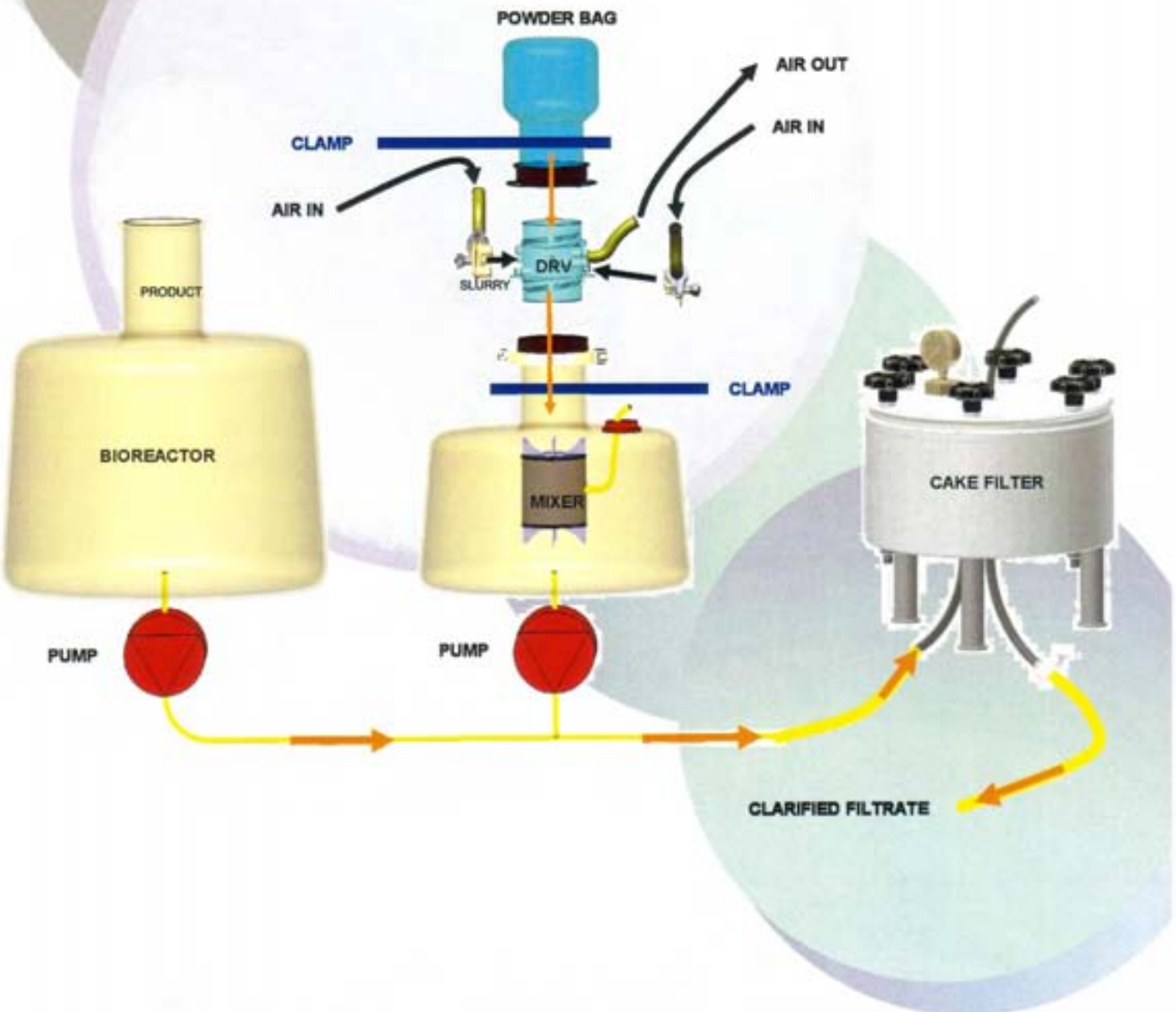
ChangeClear
Principle Configuration



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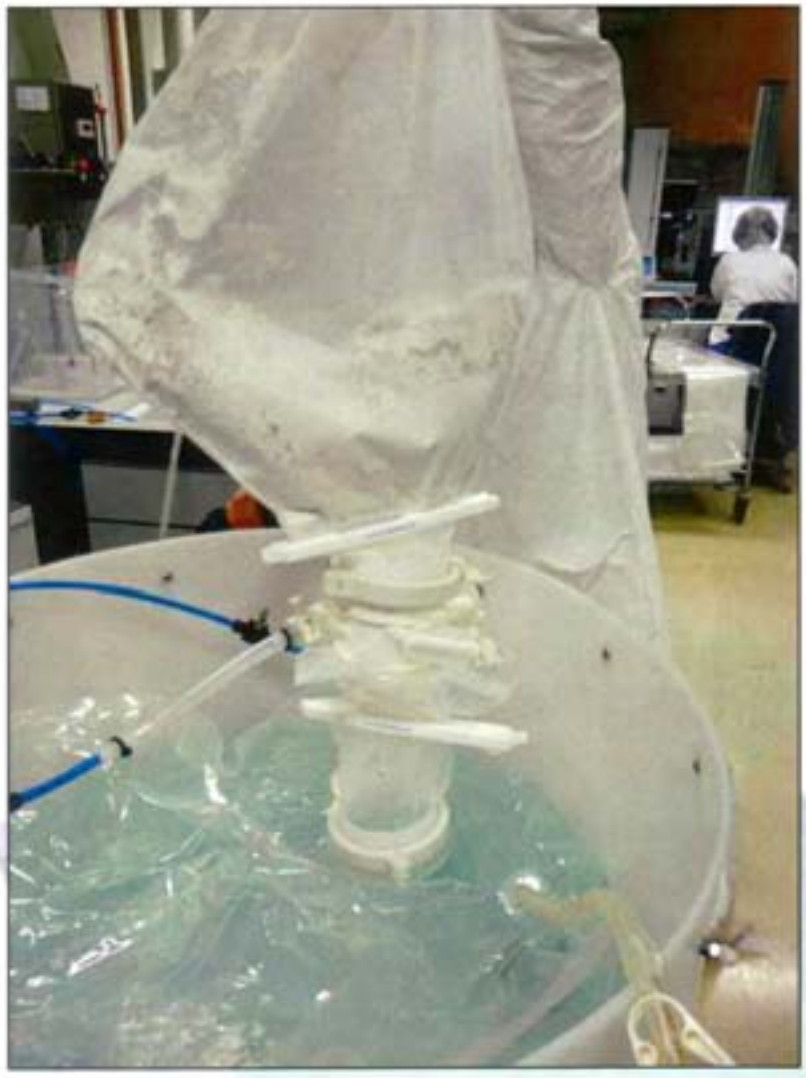
Large-scale Production System

Large-scale production is supported with a unique valve that, while disposable, prevents operator contamination.

Large-scale ChangeClear™ saves time and money by safely dispensing DE, with easy disposal, while providing a technological edge.



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