

Single-use systems and single-use technology in biopharmaceutical manufacture

Summary

Single-use systems (SUS) whose product-contacting parts consists of FDA-approved plastics are increasingly used in biopharmaceutical productions. They are predominant in upstream processing (see Figure 1), but also exist for downstream processing and Fill & Finish. Their usage has not only contributed to savings in time and money when chosen and handled correctly, SUS have entailed new technologies (e.g., large volume cell banking procedures, one step cell expansions, high seed fed batch productions, see Kaiser et al., 2015). Furthermore, they have become accepted in applications exceeding mammalian cell cultivation during last years. For example, there is growing demand for applying single-use technologies (SUT) in productions with microorganisms, insect cells and human primary cells obvious.



Figure 1: SUS often used in upstream processing (with kind permission from Sartorius Stedim Biotech)

Services and research for apliers

- Selection and bioengineering characterization of SUS: Fluid flows, mixing times, kLa values, shear stresses, identification of critical bag films by using a cell culture test (DECHEMA recommendation)
- Development and scale-up of upstream processes up to pilot scale: Cell productions, productions of antibodies and vaccines
- Customized training courses: Bioengineering characterization of single-use bioreactors, cell cultivations in orbitally shaken, wave-mixed and stirred single-use bioreactors, scale-up of bioprocesses up to 50 L working volume

Selected Publications

- Single-use bioreactors for animal and human cells. S.C. Kaiser et al., In: Animal cell culture: Cell Engineering 9, Springer, 2015
- Recommendation for leachables studies. R. Eibl et al., DECHEMA, 2014
- Single-use technology in biopharmaceutical manufacture. R. & D. Eibl, John Wiley & Sons, 2011
- Single-use bioreactors I and II. R. & D. Eibl, Springer, 2009 and 2014

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Vision

Our vision is to support suppliers to develop novel and to optimize existing SUS for the upstream processing and first steps of downstream processing (cell and product separations). Usage of both classical and also modern engineering tools (e.g., Computational Fluid Dynamics and Particle Image Velocimetry) allow reliable equipment qualifications while reducing the number of experiments. In addition, optimized equipment prototypes are designable and verifiable within shortest time. Furthermore, we can help apliers to choose the optimum SUS for their applications, to use them without any trouble and to develop and scale-up upstream production processes. We have long-term experiences in process developments based on mammalian, insect, plant and cells, but have also the knowledge to expand human mesenchymal stem cells.

Services and research for suppliers

- Bioengineering characterizations and optimizations of SUS: Mixers and bioreactors (DECHEMA Guideline), peripheral elements (filters and pumps, see Figure 2)
- Development of novel SUS: Mixers, bioreactors
- Biological tests with model cell lines (writing of application notes included): Chinese hamster ovary (CHO) cells, *Spodoptera frugiperda* cells (subclone 9, Sf-9) in combination with a model baculovirus expression vector system, Different plant suspension cell lines, *E. coli* cell line, immortalized adipose tissue-derived human mesenchymal stem cells

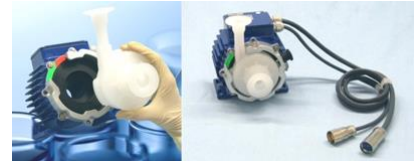


Figure 2: Magnetically levitated, centrifugal pump PuraLev (with kind permission from Levitronix). This single-use pump for shear sensitive liquids was optimized within a government-funded research project. Research partners were the company Levitronix and our group.

Collaboration Opportunities

We have carried and are carrying out projects in co-operation with companies being both suppliers (e.g., Adolf Kühner, Finesse, GE Healthcare, Levitronix, Presens, Sartorius Stedim Biotech) and apliers (e.g., Cytos Biotechnology, Laves Arzneimittel, Lonza, Hoffmann-La Roche) of SUS and SUT. In addition, we are closely linked with companies as well as research groups being members of the biotechnet Switzerland and the DECHEMA working group "Single-Use Technology".

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