

Workshop I - Platform technologies and integrative solutions

GE Healthcare



GE Healthcare

Intensify your process with perfusion

Traditionally, cell retention has primarily been used in perfusion processes when fast separation of the product from the culture has been required. Emerging strategies involve perfusion-like settings also for other applications, such as monoclonal antibody production, seed-train, and cryopreservation. This workshop will present various process alternatives that involve perfusion under single-use settings and provide examples of strategies for cell retention using tangential filtration.



Pall Life Sciences

Single-Use Technologies for Formulation and Filling : Considerations and Solutions.

To date single use technology has been widely adopted for upstream and downstream processes in the biotechnology sector but there has been limited uptake for formulation and filling applications due to limitations in technology. This workshop will discuss the new technology choices and show how a single use filling line can be realized, using various technology options. One of the key components of the fluid path development has been a very innovative polymeric single use filling needle. We will review key aspects of the development of this filling technology and provide data regarding filling accuracy and repeatability, with fluid of different properties & different type of dosing technologies. These needles have been used on a variety of filling machines. Validation aspects including Extractables and Leachables will be discussed as well.

Sartorius Stedim Biotech GmbH

Platform technologies and integrative solutions

Single use process solutions have changed our approach to making proteins from cell cultures dramatically. Besides classical biopharmaceuticals and vaccines, cell therapy products are moving towards industrial relevance. All this increases technical, supply chain and quality requirements on single-us bioreactors and processing solutions significantly.

Whilst single-use solutions for contained media, buffer and intermediate handling and storage are well established, more and more companies are adopting single use bioreactors in production up to and beyond the 1000 L scale. Especially continuous processing has gained tremendous interest in recent years as it allows reducing production scale and facility footprint. Driven by a growing pipeline of biopharmaceutical drugs in development and the cost pressure that the Pharma industry is experiencing, further efficiency gains can be achieved by using single-use bioreactors in process development in combination with Design-of-Experiment tools to streamline process development and validation. To mitigate risks associated to scale-up and process transfers to existing facilities, it is crucial to understand critical performance criteria of the employed bioreactor systems, e.g. mixing behavior, oxygen transfer and CO₂ removal. Additional chemometrics tools such as MVA online help to monitor process behavior and enable root cause analysis of potential deviations.

During the workshop we will discuss the current status of single-use bioprocessing solutions including novel connection technologies and improvements in process automation and control. Further emphasis will be on DoE, scale-up, high cell density cultures and risk mitigation tools such as bag testing.

Workshop II - Platform technologies and integrative solutions



ATMI LifeSciences

The Source for Bioprocess Efficiency™

ATMI LifeSciences is the source of bioprocess efficiency, providing a broad range of innovative single-use technology products and services that maximize product integrity, support bioprocess development efforts and optimize manufacturing costs.

Innovation is at the heart of ATMI LifeSciences' mission to deliver advanced bio-process efficiency solutions. Our innovative, market-leading and fully integratable portfolio of single-use bioreactors, mixing and storage systems is driving bioprocess efficiency and delivering value for biopharmaceutical companies around the world:

- Ultraclean sterilizable and breathable Packaging – Newform™
- Integrity® single-use mixers, the largest installed based units used for upstream and downstream applications, in cGMP environments
- Integrity® single-use bioreactors designed to simplify and intensify fragile cells, virus and protein production processes
- Integrity® single-use liquid/power storage, dispense and transport vessels
- Helium integrity platform (HIT™), helium-based testing system designed to detect defects as small as 10 microns in single-use assemblies, immediately before use

In addition, an expert team of scientists and application specialists is available to support our customers efforts on-site or in one of our bioprocess development labs. Along with the advanced Integrity® line of mixers, bioreactors and storage systems, ATMI capabilities help our customers succeed in their cell culture process optimization and scale-up.

During the workshop “Platform Technologies and Integrative Solutions”, our expert will share his insight on single-use for biomanufacturing, and how ATMI technologies help to overcome the related challenges to reach process efficiency and standardization.



Meissner Filtration Products, Inc.

Clarification as an Integrated Single-Use Solution

As biopharmaceutical production processes harness more and more the potential of single-use process steps, it is often desired for reasons of process efficiency and simplification to provide an integrated process solution. One such integrated process solution for example is clarification where single-use filter elements are combined with fluid handling in a ready-to-deploy assembly. The cornerstone of the filter system is a novel assembly module, UltraSnap™ which configures multiple UltraCap® heavy duty capsule filters in an application specific array. Individual filter elements can range in size from 10" to 50" and each capsule filter can be optimized for filter medium and pore size. A single-use integrated UltraSnap™ clarification system would typically consist of one or more depth filters followed by prefilter and/or sterilizing grade filters. The system readily scales with the process volumes contemplated. Overall an UltraSnap™ filter assembly eliminates the time and expense associated with change-out of filters from stainless steel housings and the associated cleaning and reassembly of the filter/housing unit(s). This time saved from cleaning operations results in less downtime between harvest steps, and improves productivity. Process simplification is enabled by virtue of the inherent system flexibility in an all integrated pre-sterilized module ready for immediate deployment. The UltraSnap™ filter assembly has very low hold-up volume, which minimizes product loss during change-outs and ensures maximum product recovery. In the workshop we will demonstrate an UltraSnap™ assembly configured for clarification encompassing a novel gamma stable ALpHA® G depth filter, a Protec® double layer prefilter and a SteriLUX® sterilizing-grade PVDF filter.



Merck Millipore

Implementation of Single-Use Technologies to Improve Speed to Clinic – Case Study Examples

With over 500 monoclonal antibodies (MAbs) in Preclinical and Phase I stages, speed to clinic continues to be a critical factor for commercial success. While the potential for single-use technologies to provide benefits in terms of reduced facility build and operating costs is now widely recognized, published performance data is still fairly limited with respect to complete single use processes.

In this workshop we aim to provide an holistic viewpoint and will use real case studies to explore the benefits that may be realized through the utilization of single-use technologies in both upstream and downstream processes. Performance data will be presented on the comparison of single-use with multi-use stainless steel bioreactors together with a discussion of approaches to attaining a fully closed process. In the downstream area we will discuss the benefits of a pragmatic approach to process development coupled to single-use pilot scale implementation to shorten time to clinic.



Thermo Scientific

Single-use bioreactor turnkey open architecture

The Thermo Scientific™ HyPerforma™ Single-Use Bioreactor is a market leading bioreactor in stirred tank design. We have hundreds of installed systems worldwide used to grow numerous cell lines in a variety of processes. The bioreactor consists of a stainless steel outer container and a single-use bag assembly. The system can be ordered either in an open architecture format or as a turnkey system. The open architecture design allows customers to: integrate with any control platform on the market; plug-and-play through standard disposable connectors; avoid the costs of investing in an additional control system; and have the ultimate flexibility to choose the control platform they want. Get your turnkey solution using the control platform of your choice for either cGMP or non-cGMP applications.

Workshop III - PAT enabling concepts and single-use sensors



C-CIT

C-CIT presents the handling and data management for in-situ Glucose sensors for cell cultures. In the workshop a shake flask will be filled with cell culture media and a sensor will be mounted to it. We then start with measurements and show the handling of the software.



Finesse Solutions LLC

Universal controllers change the way to plan a R&D laboratory or process development work. Points of control can now be defined which have flexibility of running either stirred vessels or rockers with either electrochemical sensors or single-use ones. Mass flow controllers have been implemented for more precise gas control and full historization of all process parameters. Supervisory software can be used to overlay on existing equipment and fully harmonize both old and new controllers. We will discuss how to set up a highly flexible and scalable laboratory for greater efficiency and power design of experiment capability.

Sartorius Stedim Biotech GmbH

Application of single-use Sensor Technologies as PAT Tools for robust biopharmaceutical manufacturing and efficient bioprocess development

Reduced time to market as well as decreased development and production costs are central issues in biopharmaceutical processing. During the past decade, modern biopharmaceutical production processes have changed due to the introduction of new technologies such as single-use bioprocessing unit operations and overall performance improvements, e.g. higher titers.

The increased use of single-use technologies results in a strong demand for reliable single-use sensors to enable application of Process Analytical Technology (PAT) as basis for effective automation and optimization of existing and new developed production processes.

PAT implicates the use of various measurement and control devices and hence needs a commitment to sophisticated automation solutions. Sartorius as a leading solution provider for single-use technologies is focusing on further developing its comprehensive single-use PAT portfolio by implementing standardized sensor and automation platforms along the biopharmaceutical production chain and from early process development up to commercial production. Sartorius PAT solutions enable smart process transfers and cost optimized production of biopharmaceuticals.

In this workshop automated applications based on latest single-use sensor and automation technologies from the Sartorius BioPAT® Toolbox like inline single-use biomass and online single-use glucose-lactate measurement for automated monitoring and control of cell culture processes will be demonstrated. Besides inline single-use pressure and flow sensors not only for media and buffer prep but also for virus inactivation, crossflow-, ultra- and diafiltration will be presented.



Sysmex Digitana AG

Sysmex is presenting Andrew™, a novel pipetting robot using conventional pipettes. Additionally, an intelligent monitoring system for cell cultures is discussed: Cytomate enables life recording of cell cultures and provides real-time information on cell numbers, confluence, doubling time and temperature. Finally, the new generation of Chemometec's NucleoCounter – the NC-250 - will be shown.

Workshop IV – New single-use systems



3M

Emphaze™ AEX Hybrid Purifier: A New Bioprocess Purification Platform Integrating Anion Exchange Hydrogel Chromatography and Size Exclusion Membrane Into a Single-Use, Scalable Device Format

3M Purification introduces the Emphaze™ AEX Hybrid Purifier, a new product delivering a high chromatographic charge capacity in a single-use format designed for superior clarification upstream of capture chromatography. An overview of the hybrid product design is presented, comprising a high-capacity, Q-functional nonwoven media and a highly asymmetric, 0.2 micron bioburden reduction membrane. Data from pure and mixed component challenges are presented to illustrate a number of the product's differentiated performance features including superior turbidity, DNA, HCP, endotoxin, and bioburden reduction. Scalable product formats, from laboratory development scale to large manufacturing scale, are outlined. Potential benefits are discussed, including best-in-class protection of the affinity capture column, reduction of post-capture impurities, and reduction of downstream polishing chromatography needs.



Filtrox AG

FILTRODISC BIO SD™ - single use liquid / solid separation

Clarification of fermentation broths is one of most important steps in downstream biotech processes.

Optimized fermentation processing leads to dramatically increased cell densities over the recent decade. Standard technologies (centrifugation, depth and membrane filtration) can no longer handle the high particle loads in an economical way. Membranes are very cost intense and their scale up is not practical. The required footprint for standard depth filtration increases with the particle load. Centrifugation, an application in which mechanical stress is applied to cells, increases the turbidity through fine particles which have to be removed further downstream in separation and purification. A depth filter with higher capacity per area would solve the issues.

Alluvium filtration is a well-established method in pharmaceutical industries. Until recently, however, it has not been used for cell separation as it was unavailable as a scalable and disposable solution with all validation requirements. FILTRODISC BIO SD is the first depth filter using the advantages of the alluvium technology in a disposable format. It is further useful for other applications like activated carbon removal or similar processes creating high cleaning requirements.

Filtrox AG will show the new FILTRODISC™ BIO SD filtration system which removes particles (e.g. cells, bacteria, yeast) and other turbid matter (e.g. activated carbon) from process liquids like fermentation broth. This system is completely disposable. This “disposability” or “single use” reduces cross contamination risks, cleaning validation efforts and reduce the downtime during module changes, making this method the ideal choice for contract manufacturers (CMO) and other operations with a high frequency of product change.

The system is scalable from lab size to industrial size filtration. The transfer from the method development stage to large scale processes can be easily achieved.

For the alluvium filtration the Pharma grade DE (Celpure an Advanced Minerals brand) will be provided from FILTROX in single use transfer bags. These can be easily connected direct to the single-use fermenter or mixing device. The DE and the cells perform a filter cake and extend the filtration time and avoid blocking of the filter media. After the filtration is done the remaining liquid from the bag can be pumped over a FILTRODISC BIO SD 5” capsule to recover the valuable liquid. After both filtration are finished both the module and the capsule can be disposed.



Levitronix GmbH

Pumps are used in the biotechnology industry for various applications in up- and downstream processes, where sterile conditions as well as smooth and gentle conveyance of the liquid media have to be realized. In single-use applications, peristaltic pumps are commonly used, but these pumps have several undesired characteristics, including low maximum flow rates, pulsating flow and pressure, alterations to the tubing material, tubing failure and local shear stress peaks. This could lead to loss of biological functionality and cell disruption, potentially resulting in the release of cell components and enrichment of cell debris in the culture broth. Low-shear pumps are therefore required for animal cell culture processing.

In the workshop a new pump technology applying magnetic levitation -MagLev Pumps- will be introduced and live demonstrations will enable the audience to see advantages and characteristics to this new technology. In addition a newly introduced reusable Ultrasonic Clamp-On Sensor will be combined with the pump system and a highly dynamic and fully automated controlled fluid system will put on stage for critical audience review and discussion.

Pall Life Sciences

The XRS 20 Bioreactor: A high performance, state-of-the art, cell-culture system for single-use applications

The XRS 20 is a high performance, state-of-the art rocker style bioreactor designed to meet the exacting demands of cell culture made by the bio-pharmaceutical industry. The workshop allows demonstration of the main features of the entire bioreactor system, including its agitation, control system and the disposable elements of the cell culture environment.

The single-use biocontainer has a volumetric operating range of 2 – 20 L, which along with the pH and O₂ optical sensors, are supplied irradiated, in light-proof foil with an inner sanitary layer. The biocontainer can be removed from its packaging, fully-connected and ready for use in a matter of minutes. This involves the installation of the main liquid addition lines for media and reagents, routing of the inlet and exhaust air lines, spare injection port, sampling line, drain line and optical sensor ports. The biocontainer is labeled with all relevant information to allow complete batch recording and traceability.

An exhaust gas filter heater maintains filter efficiency over extended periods of use, whilst culture temperature is carefully controlled by a combination of a heating mat, insulation provided by the fully enclosed reactor environment and a vent fan.

The control tower has touch screen functionality, three peristaltic pumps for aseptic fluid management, gas management, USB ports and rear OPC connection. Touch screen operations are fully embedded and include: synoptic and summary views where agitation, heating, gas flow, pH, and dissolved O₂ can all be managed to suit the needs of the individual cell culture. Furthermore, trend screens, cascades and recipes can all be accessed to ensure optimal management or review of the cell culture.

When fully inflated the biocontainer is ready for use and effective mixing of the cell culture media can proceed. The XRS 20 platform is equipped with safety locks, auto-resume function and a readily visible emergency stop. The bi-axial rocker style motion ensures maximum efficiency of mixing in the culture environment resulting in highly productive cell cultures.

Taken together, the functionality of the XRS 20 unit, control tower and biocontainer represent a highly effective cell culture system with class-leading performance for application in lab, research, pilot- and full-scale manufacturing environments.

Workshop V – Cost modeling



BioPharm Services Ltd.

Analysing how an integrated disposable process can increase productivity, significantly reduce costs and bring products to market faster

With the drive to reduce the cost of drugs and the rise of biosimilars, the focus is on cost reduction throughout the product lifecycle. The BioSolve Process modelling platform, now in its 5th year allows users to rapidly evaluate the impact of process options and of innovative new technologies such as disposables on processes in development, scale-up, tech transfer and commercial manufacturing.

This workshop will provide insight into the key functionalities of the BioSolve process modelling platform, and will demonstrate how to model a process and use that to identify opportunities to increase productivity and reduce Cost of Goods. This is demonstrated through a case study using BioSolve Process to demonstrate how quickly you can determine the right mix of disposable technologies for any given process and scale. This will be backed up by reference to industry end-user case studies by Merck, Sanofi Pasteur, J&J Crucell. These and other companies use BioSolve Process to evaluate when and where it makes sense for them to work with innovative technologies such as disposables. A case study from the Pierre Fabre new clinical trials facility will demonstrate how BioSolve Process was used to support the rapid design of a multi-product flexible facility design based on the latest disposable technologies.

Sartorius Stedim single-use products Biostat, FlexAct for different applications, AEX with Sartobind, Virosart, Sartocube, Sartopore and Celsius Pak have been modelled with the BioSolve framework. Working with their Process4Success mAb platforms Sartorius will demonstrate the impact of the given technologies on different processes at different scales within the Process4Success platform.

The workshop will finish with a quick review of some of the latest new features of the BioSolve platform including its applications to

- Continuous Processing
- Facility fit
- NPV analysis
- Collaborative working