CBP-Continuous Bioprocessing of Biomolecules

Overview

For synthetic APIs, increasing attempts to move from traditional batch to continuous manufacturing are ongoing. Advantages besides lower CAPEX und OPEX are in particular higher product safety by enhanced process robustness, smaller foot print of the plants, lower cleaning costs and downtimes due to dedicated modular and flexible plants.

In manufacturing of biomolecules these concepts have so far only been applied for high-volume bulk or fine chemicals. However, with the upcoming cost issues in the manufacturing of biotherapeutics by low cost biogeneric manufacturers and stratified medicine scenarios, first approaches to industrialize continuous manufacturing for biologics like amino acids, peptides, proteins and monoclonal antibodies and fragments, are under investigation.

For the production of biopharmaceuticals, e.g. monoclonal antibodies, fermentation is already more often used in a continuous perfusion mode than is known to the public. Therefore, it is only consistent to apply continuous process concepts also for Downstream Processing operations. However, until recently the necessary unit operations and corresponding equipment has not been available. This is currently undergoing through a substantial change. Besides a broad variety of continuous chromatography applications with or without protein A, also older well known unit operations like liquid-liquid extraction processes based on ATP (Aqueous-Two-Phase) systems or precipitation by aid of suitable auxiliaries have become available and begin to find their place in a full continuous process scheme.

To accelerate slower unit operations better system performance, e.g. in chromatography, rod- or radial chromatography columns together with modern packings, as well as membrane adsorbers in IEX- or HIC-mode are available or under development.

The role of single-use (SUS) / disposable concepts, which are more and more applied also in industrial scale up to 2000 L volumes, in a fully continuous operation have yet to be defined. Their fields of use will depend on an individual processrelated economic assessment.

New developments in manufacturing equipment, including analytics, as well as new process design concepts based on QbD-approaches can only be successfully integrated into efficient, reproducible, and robust continuous processes by the combination of modeling and simulations with laboratory-scale experiments.

The course will describe the design and scheduling of unit operations in continuous manufacturing processes in contrast to classical batch operations and aims at providing viable decision criteria.
Scientists and laboratory technicians, involved in process development and / or piloting / manufacturing will be trained how upstream and Downstream Processing sequences are efficiently scaled from preparative to pilot and production scale. Profound theoretical and experimental knowledge as well as comprehension of newest design methods will help to manage the time pressure and enormous experimental efforts in daily project work.

Who Should Attend:

Scientists and laboratory technicians, involved in process development and / or manufacturing. Besides some basic knowledge in computer handling no previous knowledge will be assumed.

Course Material and Infrastructure

Each participant will be provided a manual with all lectures at the beginning of the course. The experimental part will be offered in the laboratories of the Institute. For the simulation tutorials laptops are provided. The experiments will be made in groups of about 2-3 participants.

Learning Objectives:

After the course each participant should be

- able to apply modern up- and Downstream Processing and process design Methods in their daily project work
- familiar with handling of continuous membrane, extraction, precipitation and chromatography equipment
- capable to evaluate platform-technologies and the consequences of the „Process Analytical Technology“ (PAT) initiative from „American Food and Drug Administration“ (FDA)
- able to lay out experiments for design of membrane, extraction, distillation, crystallization / precipitation and chromatography processes
- capable to perform a scale-transfer for unit operations into pilot and manufacturing processes
- well informed about possibilities and limitations of process design and CBP unit operations by aid of simulation

21 Aug 2017

Tuesday, 27 February 2018

19:00	Check-In and Dinner in Restaurant "Pixhaier Mühle"
20:00	Oberharzer Wasserregal and Mining History

Wednesday, 28 February 2018 8:30 – 24:00

8:00	Welcome and Introduction
8:30	Fundamentals Continuous Bio-Chromatography
9:15	Design of ContiBioChrom
10:15	GMP Regulatory Continuous Bioprocessing (CBP)
11:15	Lunch
12:00	Quality by Design (QbD) - Technology in Downstream Processing (DSP)
12:45	Lyophilization
13:30	CBP – Industrialization
14:15	Process Analytical Technology (PAT) and Bioanalytics, Regulatory
15:00	Discussion and Course End
19:00	Dinner Restaurant „Glück-auf"
21:00 - 24:00	Midnight Session at "Pixhaier-Mühle": Simulation Tutorials Batch and Conti-Biochromatography

Attention:
These Agenda Topics overlap with DSP - Purification of Biomolecules Training Course

Thursday, 1 March 2018 8:30 – 14:30

8:30	Continuous Bioprocessing (CBP) Fundamentals
9:15	CBP batch to conti – cost studies
10:15	Tutorial: CBP Total Process Studies
11:15	Lunch
12:00	Guided Tour Institute
13:00	Case study CBP for MABs
13:45	QbD studies
14:30	Course End and Discussion

Modifications of the Program are possible.