CONTINUOUS MANUFACTURING
Development, Production and Quality

4/5 December 2019, Berlin, Germany

MODERATED BY
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Nasr Pharma Regulatory Consulting & formerly FDA

SPEAKERS
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Sanofi

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DR CHRISTOPH WABEL
Pfizer

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MSD

HIGHLIGHTS:
- Regulatory requirements for continuous processes
- Authorities expectations for CM
- Adaption of the Pharmaceutical Quality System
- Operational Quality Assurance aspects
- Available Equipment & Technology
  - Continuous Bioprocessing
  - Continuous OSD Manufacture
- Control Strategies for Continuous Processing
- Case Study Vertex: Implementation of Real-Time-Release-Testing
- Case Study Pfizer: Continuous OSD Manufacturing
- Case Study MSD: Continuous direct Compression
- Case Study Sanofi: Continuous Chromatography (DSP)

This conference is recognised for the ECA GMP Certification Programme „Certified Technical Operations Manager.“ Please find details at www.gmp-certification.eu
It is the aim of this conference to show how a transition from batch to continuous manufacturing can look like. Questions regarding technology, process development and GMP/Quality Assurance and Regulatory Affairs will be discussed.

Solid dosage forms are still the most common dosage form, first and foremost tablets without any pioneering developments in the recent years. But driven by only a few pharmaceutical companies more and more of the global players started to invest in continuous manufacturing (CM). Companies like GSK, Pfizer; Johnson & Johnson and Vertex have been in the news lately. But also the Biotech Industry started to invest in CM. Upstream Processing is the more common area, but lately also Downstream Processes have been developed to be run continuously.

A shift from batch to continuous manufacturing could be one of the largest paradigm changes since the system of validation & qualification came up years ago.

Continuous manufacturing is data driven and by gaining this flood of information two topics become very important: process control and process monitoring. A vast amount of data has to be evaluated in order to control the process and to decide whether material can be collected or has to be rejected. This fundamental shift is also a major challenge for the Quality Unit. The Quality Management System has to be adapted to also cover continuous processes.

Regulating authorities, first of all the FDA, also encourage the transition from batch to continuous production. They expect an increase in product safety while equipment suppliers promote a decrease of production costs. But with a continuous mode of operation new questions raise:

- How should a batch be defined? Is there a difference between lot and batch?
- What new risks does a continuous process involve?
- How can a continuous line look like?
- How can a continuous process be kept in a controlled state?
- How is a continuous system validated?
- How to determine the Residence Time Distribution – what about material traceability?
- How should deviations in a continuous process be handled?
- How should equipment cleaning and maintenance be scheduled?
- Which documents do the authorities require for approval of continuous processes?

Listen to companies who already did the transition and learn how they answered the questions above.

This conference is directed at
- Decision makers dealing with the question whether continuous manufacturing is suitable
- Executives from development, engineering, production and QA responsible for the implementation of continuous manufacturing

Dr Moheb Nasr, NPRC and formerly FDA

A Global Perspective on Regulatory and Quality Consideration of Continuous Manufacturing

- Impact of current regulatory system on implementation of CM
- Points to consider prior to the implementation of CM
- Filing requirement and expectations – Global perspective
- Remaining regulatory challenges
- Future regulatory guideline – ICH and regional

Authorities’ expectations regarding continuous processes

- Critical elements & considerations when filing an MAA
- Regulatory guidelines and assistance in the EU
### Development & control of continuous Processes

- Determining the extent of RTD and implementing as part of control strategy
  - Explanation of control strategy complexity pyramid
  - Introduction to performance based control
  - The role of process dynamics in performance based control
  - When and where to apply residence time distribution (RTD)
  - Setting action limits based on performance based control
  - Using performance based control data as part of a real-time release strategy

- Real Time Release Testing and Drug Product Continuous Manufacturing
  - Implementation considerations for a control strategy including RTRT will be reviewed.
  - Differences between IPCs and RTRT in drug product continuous manufacturing will be discussed.
  - Approved real time release testing approaches will be described.
  - Possible next steps in the evolution of RTRT and CM will be presented.

### Quality Assurance for continuous Manufacturing

- The Quality Journey to Continuous Manufacturing
  - Changes in the in the Quality Management System
  - Implementing Control strategy
  - Preparing for Real Time Release

- Installation of a CM line at Janssen from a Quality point of view
  - Equipment Qualification
  - Handling deviations
  - Implementation of the CM process in an existing development plant

### Technology & Equipment

- Process Solutions for OSD manufacture
  - Continuous Solid Dose Manufacturing- Review of Process Options
  - When to use which process options
  - Review of
    - Lose in Weight Feeding
    - In line mixing
    - Continuous wet granulation and drying
    - Tablet Compression
    - Continuous Coating

- Continuous Processing for Biopharmaceuticals
  - Overview of continuous bioprocessing concepts for biopharmaceutical products
  - State-of-the-art in continuous bioprocessing concepts
  - Possibilities and challenges of continuous manufacture
Case Study Sanofi: Use of continuous chromatography for downstream processing of biologics – benefits and challenges

- Review typical downstream purification process for therapeutic antibodies
- Application of continuous chromatography in downstream processing of therapeutic antibodies
- Benefits regarding cost of goods, throughput for different stages of the project – clinical supply vs. commercial supply
- Presentation of two case studies showing upscale of processes from development labs to production facility:
  - mAb A
  - mAb B
- Challenges during use of continuous chromatography, e.g. stability of load material, sanitization of resins, bioburden
- Application to fed-batch processes vs. perfusion processes
- Knowledge sharing based on implementation under GMP at sanofi-aventis

Case Study Pfizer: Continuous OSD Manufacturing

- Reasons for Continuous Manufacturing
- Regulatory Specifics
- Special Consideration during Development and Routine
- Controlling continuous processes
- Handling of deviations during production

Case Study MSD: Continuous Manufacturing using Direct Compression

- Experiences with developing, commercializing, and filing MSD’s first CM product.
- Use of an RTD Process Model for Rejection in a CDC process.
- Look-ahead towards future innovations with Continuous Manufacturing

SOCIAL EVENT
In the evening of the first conference day you are cordially invited to a social event. This is an excellent opportunity to share your experiences with colleagues from other companies in a relaxed atmosphere.
DR FLORIAN CAPITO | Sanofi | Lab Head Bioprocesses & Manufacturing at Sanofi-Aventis
Since 2015 Florian Capito is leading a DSP Development lab at Sanofi-Aventis Deutschland GmbH, developing purification processes for biologics. Before he was involved in process characterization studies at Sandoz, focusing on chromatography and UFDF steps. Florian has a PhD in Chemistry and a Master in Protein science.

DR NICK LEE | Health Product Regulatory Agency (HPRA), Ireland | Executive Pharmaceutical Assessor
Nick Lee is an Executive Pharmaceutical Assessor in the Health Products Regulatory Authority of Ireland where he is the department lead for Continuous Manufacturing. He is also the IE delegate to EMA’s QWP and a member of the EMA PAT Team. Prior to joining the HPRA, Nick spent over 15 years in Industry in increasingly senior roles.

BRITTA MANSER | Pall Biotech | Manager of Continuous Bioprocessing
Britta Manser obtained a master's degree in pharmaceutical biotechnology from the Zurich University of Applied Sciences. As manager of continuous bioprocessing in Europe at Pall Biotech she is heading a team focusing on the development, implementation and integration of continuous processing.

DR JOSEPH MEDENDORP | Vertex Pharmaceutical | Director at Vertex Pharmaceuticals
Joseph Medendorp is a Director of Technical Operations Analytical at Vertex Pharmaceuticals, focusing on new product commercialization and lifecycle management of current commercial production. The group is responsible for maintaining the spectroscopic and soft-sensor IPC and RTRT methods used on the Vertex CM platforms.

DR MOHEB NASR | Nasr Pharma Regulatory Consulting & formerly FDA | Principal at Nasr Pharma Regulatory Consulting (NPRC)
Moheb Nasr managed the CDER Pharmaceutical Analysis Program at the US FDA for four years and had the lead of the CDER/FDA CMC Regulatory Program for more than eight years. He also worked for GSK as VP Global CMC Strategy. In 2018 he started his own consultancy business.

ILSE NUYENS | Janssen Pharmaceutica | Manager Quality Assurance Compliance & Projects
Ilse Nuyens is working in the Quality organization of Janssen Pharmaceutica. She is member of the core team to introduce the Continuous Manufacturing Line into the clinical production plant in Beerse, Belgium to ensure quality oversight and process understanding for CM.

DR HARALD STAHL | GEA | Vice President & Head of Application Development and Strategy
Dr Harald Stahl started his career in the Pharmaceutical Development of Schering AG in Germany. Since 1995 he served within GEA Process Technology in various positions. Presently he owns the position of a Vice President and is Head of Application Development and Strategy. He has published more than 20 papers on various aspects of pharmaceutical production.

ILSE VANNUFFELEN | Janssen Pharmaceutica | Director Quality Integrator, Product Quality Management
Ilse Vannuffelen is Director Quality Integrator for New Products in development within the global Product Quality Management organization. Ilse Vannuffelen is subject matter expert continuous manufacturing for the Quality integrators.

DR CHRISTOPH WABEL | Pfizer | Director/Team Leader Process Management, Product and Process Development
Dr Wabel is a pharmacist with an MBA from University of Reading, UK. He heads the team of technical project managers responsible for co-development and tech transfer of new solid oral dose products at the Pfizer, Freiburg site. He has 21 years of experience in development, scale-up and global launch of new solid oral drugs.

MARTIN WARMAN | Martin Warman Consultancy | Director
Martin has an experience of 25 years in the development and implementation of PAT. He was leader of PAT Development at Pfizer Global Manufacturing and has spent seven years at Vertex where he was the technical lead for the Vertex DLR platform. Martin is also on the Exec Committee of ASTM E55 that covers pharmaceutical manufacturing and chairs ASTM E55.01 covering PAT.

FRANK WITULSKI | MSD | Director of Engineering
Frank is a Director of Engineering in MSD’s Pharmaceutical Commercialization Technology department and holds a Master of Science in Chemical Engineering. He has over 19 years of experience in process and packaging development and commercialization of OSD products, and has spent the last 4 years leading the group responsible for commercializing MSD’s first continuous direct compression process.
Date
Wednesday, 4 December 2019, 09.30 – 18.00 h
(Registration and coffee 09.00 – 09.30 h)
Thursday, 5 December 2019, 08.30 – 15.30 h

Venue
TITANIC Hotels Berlin
Chausseestrasse 30
10115 Berlin, Germany
Phone: +49 (0)30 311 6858-0
email: Info.tbc@titanic-hotels.de

Fees (per delegate plus VAT)
ECA Members € 1,590
APIC Members € 1,690
Non-ECA Members € 1,790
EU GMP Inspectors € 895

The conference fee is payable in advance after receipt of invoice and includes conference documentation, dinner on the first day, lunch on both days and all refreshments. VAT is reclaimable.

Accommodation
CONCEPT HEIDELBERG has reserved a limited number of rooms in the conference hotel. You will receive a room reservation form/POG when you have registered for the course. Reservation should be made directly with the hotel. Early reservation is recommended.

Registration
Via the attached reservation form, by e-mail or by fax message. Or you register online at www.gmp-compliance.org.

Conference language
The official conference language will be English.

Organisation and Contact
ECA has entrusted Concept Heidelberg with the organisation of this event.

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For questions regarding content please contact:
Dr Robert Eicher (Operations Director) at +49-62 21/84 44 12, or per e-mail at eicher@concept-heidelberg.de.

For questions regarding reservation, hotel, organisation etc. please contact: Niklaus Thiel (Organisation Manager) at +49-62 21/84 44 43, or per e-mail at thiel@concept-heidelberg.de.

Reservation Form (Please complete in full)

Continuous Manufacturing
4/5 December 2019, Berlin, Germany

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