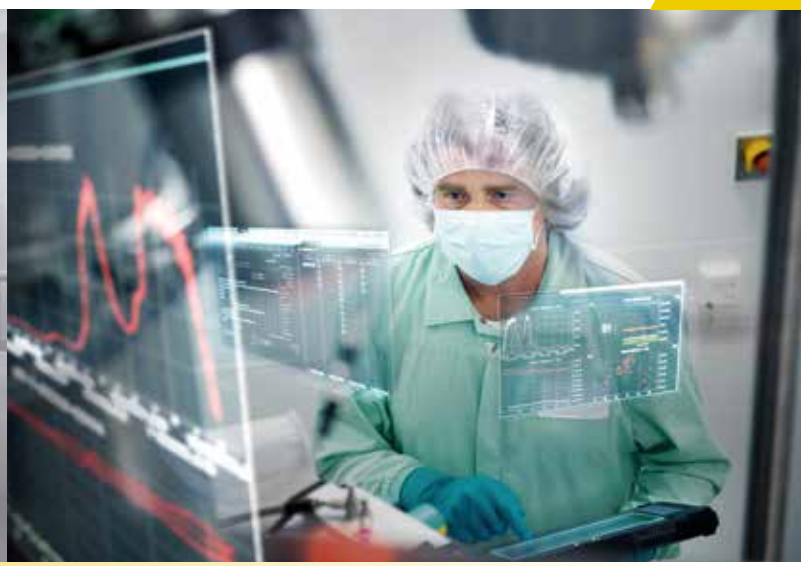
The Reality of Continuous Pharmaceutical Manufacturing



AGENDA 26-28 MARCH 2019

Taking place on 26–28 March 2019, GEA, Siemens and Perceptive Engineering will host an inaugural three-day conference to examine the fact and fiction of continuous manufacturing (CM) in the pharmaceutical industry.

The event will comprise two days of presentations from early adopters, one of which will take place at the National Formulation Centre in Sedgefield, UK, courtesy of the Centre for Process Innovation (CPI), and a chance to visit MSD's, Cramlington plant. The company has recently installed a CDC50, two ConsiGma® coaters and a Bruker Tandem, and is utilising Siemens PAT technology.

With an expected attendance of 80–120 delegates and focusing on the real-life experiences of existing users of CM technology in the development and manufacture of oral solid dosage (OSD) forms, topics on the agenda will include the current status of "going conti" as well as future plans and expectations.

Confirmed speakers include representatives from
• AstraZeneca • Bayer • CMAC • GSK • Janssen • Merck • RCPE • UCB Pharma • University of Sheffield.

CONTINUOUS MANUFACTURING

Now gaining momentum in the pharmaceutical industry, CM presents a new approach to OSD form production and meets the industry's demands for faster product development, reduced costs and increased manufacturing flexibility.

Providing higher yields, lower utility consumption and reduced waste, CM is enabling drug makers to move away from stepwise and time-consuming batch processing to a fully integrated and closely controlled process that gives excellent product consistency by intrinsic design.

The use of CM technologies and inline PAT monitoring is a key driver of building quality by design (QbD) into the complete product lifecycle, from R&D through to manufacturing, with the ultimate aim of getting safer medicines to market in a more efficient and cost-effective way.

Using model-based supervisory advanced process control (APC) to capture unique equipment, material and PAT characteristics creates a system that increases precision and optimizes the yield, capacity and OEE of the CM equipment.

Environmentally friendly with a much smaller footprint, CM is helping the pharmaceutical industry to produce higher quality products, enhance drug safety and reduce its industrial footprint, which provides significant advantages to governments, companies and patients alike.

GEA engineering for a better world

PERCEPTIVE ENGINEERING

SIEMENS Ingenuity for life

The Reality of Continuous Pharmaceutical Manufacturing
SPEAKERS

USER EXPERIENCES AND THE CURRENT STATUS OF CONTINUOUS PHARMACEUTICAL PROCESSING TO BE ADDRESSED DURING A THREE-DAY EVENT NEAR NEWCASTLE, UK

Development and Control Strategies for a Continuous Direct Compression Process

Bernd Van Snick, *Scientist, Continuous Manufacturing* – **Janssen**

The presentation will highlight the current state of continuous manufacturing within Janssen, including an overview of milestones, available continuous manufacturing platforms, academic collaborations and the deployment strategy. In addition, the general development and control strategies for a continuous direct compression process will be presented. Focusing on the encountered challenges and sharing how these were mitigated during drug product development. The various control strategy elements will be discussed including calibration and verification of a residence time distribution process model, initial findings on the process analytical tools and a strategy for determining the frequency of in-process control sampling.

GSK R&D Perspectives of PAT for Continuous API and Drug Product Manufacture

Ian Barylski, Scientific Leader R&D PAT team – **GSK**

In common with most other pharma companies GSK is developing continuous processes for both API and drug product manufacture. This presentation will give an overview of some of these processes and the PAT applied to them. The benefits, barriers to implementation and thoughts on the future direction of PAT will also be shared.

Continuous Manufacturing Research: Progress & Pitfalls

Professor Alastair Florence, *Director of the EPSRC Future Manufacturing Research Hub* – **Continuous Manufacturing and Advanced Crystallisation (CMAC)**

Continuous manufacturing is seeing increased adoption in industry with a number of products now supplied via this approach. With a wide range of capabilities available for flow synthesis, workup, crystallisation, isolation, drying, formulation and secondary processing of finished product available across lab and commercial scales there is increasing focus on the successful integration of unit operations, coupled with robust modelling, online measurement and advanced control techniques. The talk aims to provide an overview of developments in continuous manufacturing research, highlighting recent progress across continuous drug substance and drug product processing activities with updates from the industry demand led research programme at the UK Continuous Manufacturing and Advanced Crystallisation (CMAC) Manufacturing Research Hub. The challenges and opportunities arising from increased need for digital design and manufacturing methods will be highlighted as well as selected areas where scientific and technological gaps remain.

Online-monitoring of Continuous Pharmaceutical Production Processes at Bayer AG

Dr. Sven-Oliver Borchert, *Technology Expert Process Performance Improvement* – **Bayer**

Continuous processing presents a promising technology for the manufacturing of pharmaceutical products. Higher flexibility, smaller facility footprints and deeper process insight are some of the advantages of this production mode. However, compared to classical batch pro-cesses, online-monitoring of critical quality attributes (CQAs) in continuous processes is essential for a reliable operation. To this end, two examples which outline the potential of SIMATIC SIPAT for the implementation of monitoring CQAs will be presented.

1st Example: Bayer´s MoBiDiK platform focuses on the purification of monoclonal antibodies (mABs). MoBiDiK stands for modular, biological, disposable, and continuous. Single-use technology and aseptic connections between unit operations offer superior protection against bioburden ingress and other forms of contamination. Furthermore, the technology offers the potential for tight control of critical process parameters (CPPs). A high degree of automation reduces the risk of operator induced errors, thus improving quality assurance. Chromatography systems for capture and purification of the mABs are integral parts of the process. Asymmetry factor (AF) and height equivalent to theoretical plates (HETP) are commonly used as indicators for column performance. Results of an online data analysis for monitoring column integrity will be presented.

2nd Example: ConsiGma 25 is a technology platform provided by GEA for continuous production of oral solid dosage (OSD) forms. It combines the process steps: twin-screw granulation, blending, tableting and film coating. Bayer is going to use the technology in a launch facility for R&D and GMP purposes. As an important part of the quality control strategy, blend uniformity is estimated from spectral NIR measurements. In this case, SIPAT will be used to enable a process control strategy based on spectral measurements. A concept will be presented which demonstrates how Bayer is going to implement a closed-loop quality control for the continuous manufacturing plant.

The Reality of Continuous Pharmaceutical Manufacturing
SPEAKERS

Building a Facility Based Upon Continuous Manufacturing for OSD

Dr. Franco Colacino, *Process Engineering Manager* – **UCB Pharma**

Design of the continuous manufacturing line

- Review of available options for line subparts, pro and con, assembly
- Design of the control strategy in the prospect of Real-time Release implementation, considering the Drug product specification
- Design of the PAT instrumentation according to the control strategy

Design of the facility

- Room layout and facility organization for GMP manufacturing
- Utilities and HVAC
- Design of the IT architecture to manage the Continuous Manufacturing line and IPC

Lessons learned during the project execution, equipment installation and qualification, building the facility and its qualification.

NCE product development, elements of Digital Design and in silico prediction

Massimo Bresciani, *Executive Director, Scientific Operations* – **RCPE**

NCEs development takes between 8-14 years, it includes all the CMC deliverables API product design, manufacturing and regulatory submission.

How far away are we from 100% automation and are virtual or site-less trials in our immediate future? The presentation will tackle some of these and other relevant issues, such as whether digital development can complement and speed up the overall process.

Introduction to CPI and its National Formulation Centre and our Role in Enabling Innovation in this Space.

Dr Graeme Cruickshank, *Director of CPI's National Formulation Centre* – **National Formulation Centre**

Overview of capabilities developed to de-risk innovation journeys in continuous learning and spark horizontal innovation across the formulated goods sector and in particular tools to better enable understanding and control of continuous manufacture in the formulated products industry.

Continuous Manufacturing of Pharmaceutical Products: Diamond Integrated Pilot Plant Dipp- The University of Sheffield

Dr. Chalak Omar, *Research Associate, Particle Products Group* – **University of Sheffield**

Manufacturing of formulated products in the pharmaceutical industry involves a series of unit operations which are traditionally operated in batch mode. The history of research in granulation of pharmaceutical products started with limited knowledge and understanding of the mechanisms happening during the process. With the development in research in the last two decades, more and better knowledge was then gained on processing of formulated products, e.g. the creation of regime map, PAT tools and the development of characterisation techniques, etc. Nevertheless, batch mode is still known to be time-consuming, labour-intensive, difficult to control. Recently, continuous manufacture of formulated products in the pharmaceutical industry has become increasingly popular. The growing interest in continuous processing has arisen from the change in the regulatory environment and the need to reduce both R&D and manufacturing costs to improve process control and provide more affordable drugs. The University of Sheffield has made a significant investment in expanding the current facilities in the pharmaceutical powder processing to build a 2 floor pilot plant with integration of all unit operations [powder feeding, twin screw granulation, drying, milling, blending and tableting] required for the continuous pharmaceutical solid oral dosage form manufacturing. This is a continuous powder to tablet line, coupled with PAT tools, and it is used for research, teaching and training purposes in the brand new £86m flagship building 'Diamond'. This is a unique continuous powder-tablet line based within UK academia, which give students a strong hands on experience in undertaking chemical engineering experiments and reinforce the basic principles. It is also providing an exclusive platform to unite and integrate the expertise in the area of pharmaceutical solids manufacturing and address the challenges in the field.

The Reality of Continuous Pharmaceutical Manufacturing
SPEAKERS

Modelling approach to Continuous Manufacturing at AstraZeneca

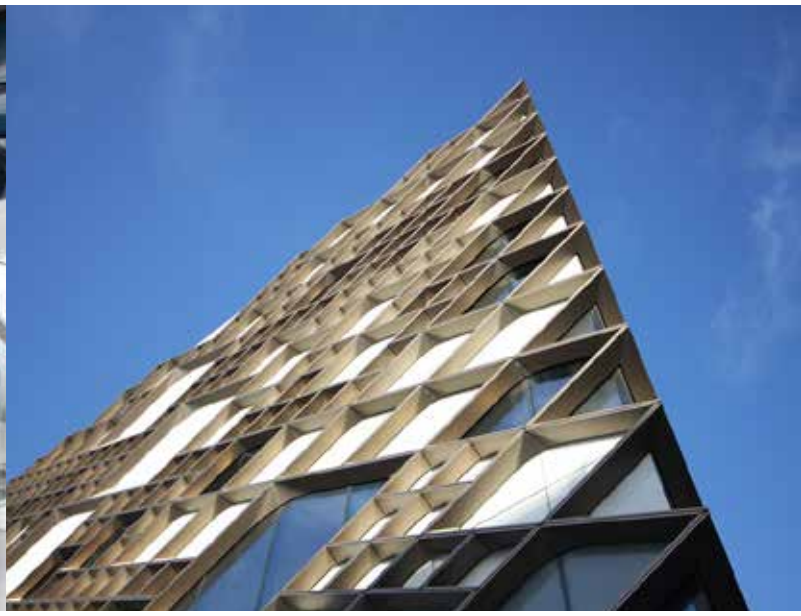
Luis Martin de Juan – AstraZeneca

Continuous manufacturing (CM) processing has attracted pharmaceutical industry attention over the last years because of advantages over classical drug batch manufacturing process such as cost-effective production and lower requirements for scale up and maintenance. Modelling and simulation plays a critical role on the implementation CM in actual drug projects by i) optimizing process design aspects, ii) reducing time and cost resulting from development of new products and iii) support of implementation of advanced process control strategies via virtual runs on integrated model systems. AstraZeneca will be presenting several examples of the modelling capability for continuous processing that has been developed in collaboration with other industries and institutions via programs such as ReMedIEs, ADDoPT, Models MPP, PROMIS Centre Consortium.

Technical Transfer from the Lab to an Integrated Continuous Manufacturing Line

– MSD

MSD, Cramlington



Diamond facility at University of Sheffield

The Reality of Continuous Pharmaceutical Manufacturing
PROGRAM

Tuesday March 26, 2019

Hotel Ramside Hall, Durham

08.00 - 09.00	Welcome coffee & registration
09.00 - 10.00	**Janssen**
10.00 - 11.00	**GlaxoSmithKline**
11.00 - 11.30	Coffee break
11.30 - 12.30	**CMAC**
12.30 - 13.45	Lunch
13.45 - 14.45	**Bayer**
14.45 - 15.45	**UCB Pharma**
15.45 - 16.15	Coffee break
16.15 - 17.15	**RCPE**
17.15 - 18.30	Free time
18.30 - 22.00	Evening event

Wednesday March 27, 2019
Track 2

Ramside Hall/National Formulation Centre

09.00 - 10.00	**AstraZeneca**
10.00 - 11.00	**MSD**
11.00 - 11.30	Coffee break
11.30 - 12.30	**University of Sheffield**
12.30 - 13.45	Lunch
13:45 - 14:15	Travel to CPI / NFC (50% delegates)
14:15 - 15:15	**CPI / NFC**
15:15- 16:15	**Guided tour to NFC**
16:15 - 16:45	Travel back to Ramside Hall
16.45 - 17.45	**TBA**
17.15 - 18.30	Free time
18.30 - 22.00	Dinner for participants of optional visit to MSD

Wednesday March 27, 2019
Track 1

National Formulation Centre/Ramside Hall

08.30 - 09.00	Travel to CPI / NFC (50% delegates)
09.00 - 10.00	**CPI / NFC**
10.00 - 11.00	**Guided tour to NFC**
11.00 - 11.30	Travel back to Ramside Hall
11.30 - 12.30	**University of Sheffield**
12.30 - 13.45	Lunch
13.45 - 14.45	**AstraZeneca**
14.45 - 15.45	**MSD**
15.45 - 16.15	Coffee break
16.15 - 16.45	Q&A
16.45 - 17.45	**TBA**
17.15 - 18.30	Free time
18.30 - 22.00	Dinner for participants of optional visit to MSD

Thursday March 28, 2019
Optional

MSD, Cramlington

08.00 - 09.00	Travel to Cramlington
09.00 - 09.30	**Registration at MSD**
09.30 - 12.45	**Guided tour at MSD**
13.00 - 14.00	Lunch

The Reality of Continuous Pharmaceutical Manufacturing
BIO'S

Bernd Van Snick, *Scientist, Continuous Manufacturing* – **Janssen**

Bernd Van Snick is a scientist in the discovery product development and supply division of Janssen Pharmaceutics, a Johnson & Johnson Company. Bernd is a subject matter expert and technical lead for developing the drug products, processes and control strategies on the continuous manufacturing platform in Beerse, Belgium. Before joining Johnson & Johnson, Bernd was at Ghent University, where he characterized GEAs continuous direct compression platform in collaboration with Janssen and GEA and got the opportunity to connect with relevant pharmaceutical partners in the industry.

Ian Barylski, *Scientific Leader R&D PAT team* – **GSK**

Ian Barylski is a Scientific Leader in GlaxoSmithKline's UK based R&D PAT team. After graduating from Loughborough University in 1990 he started his career in the pharmaceutical industry as an analytical scientist with the Wellcome Foundation, supporting the development of new chemical entities. Following the formation of GlaxoWellcome in 1996 he moved into a technology development role and delivered automated analytical tools for use by the synthetic chemistry groups, as well as gaining experience in the application of PAT in API manufacturing. Ian moved into his current role in 2012, focussing on PAT for drug product development and is the Business Owner for the SIPAT data management system for the GSK R&D organisation.

Dr. Sven-Oliver Borchert, *Technology Expert Process Performance Improvement* – **Bayer**

Sven-Oliver Borchert studied biotechnology in Hamburg with a focus on bioprocess engineering and automation. He has been a SIPAT user since 2013 and has continuously deepened his knowledge in the field of data management and data analysis. Building on this, his dissertation deals with aspects of online MVDA for sequential batch processes.

Today he is a project engineer for process performance improvement at the Bayer AG in Leverkusen, Germany and is involved in various projects concerning process design and process optimization.

Dr. Franco Colacino, *Process Engineering Manager* – **UCB Pharma**

Franco Colacino is a Process Engineering Manager at UCB and is currently in charge of the company's continuous manufacturing program. Previously a Process Engineer and Dry Form Production Team Leader, Franco has a wealth of experience in project management and pharmaceutical production. Fluent in French, English and Italian, he earned a Doctor of Science degree from the Université Catholique de Louvain and also holds a Master of Science in chemistry from the same university. He is married with two children.

Massimo Bresciani, *Executive Director, Scientific Operations* – **RCPE**

Massimo Bresciani is Executive Director at RCPE (Graz, Austria) and a scientific adviser for international life science start-ups. With more than 25 years of experience in the pharmaceutical industry, Massimo has previously held business development roles in disciplines from lead optimization and candidate selection to regulatory submissions and beyond. An advocate of personalized medicine and improving the "health experience," he is an executive board member of the Geriatric Medicine Society and has authored numerous scientific paper and patents.

Dr. Chalak Omar, *Research Associate, Particle Products Group* – **University of Sheffield**

Dr Chalak Omar obtained his PhD from the Participle Product Group at the University of Sheffield in 2017. During his PhD, he focused on Dry granulation technology to study the Roller compaction behaviour of different powders. Following his PhD, he worked in the Chemical and Biological Engineering at Sheffield university as a Postdoctoral Research Associate.

Currently, Dr. Chalak Omar is working in the Diamond integrated Pilot Plant (DiPP) at the University of Sheffield, where he is responsible for teaching and research in a State of Art laboratory consisting of ConsiGma25 powder to tablet line, continuous crystalliser, filter dryer and bioreactors.

Luis Martin de Juan – AstraZeneca

ABOUT THE ORGANIZERS

GEA has been pioneering continuous manufacturing (CM) solutions for the past 14 years and helping customers to develop, evaluate and optimize continuous processing techniques to enable them to bring new products to market faster and cheaper.

Perceptive Engineering develops and deploys advanced analytics and intelligent control systems to blue-chip clients around the world.

Siemens is a world-leading provider of digital solutions for the entire value chain and, in particular, of PAT data management platforms for continuous pharmaceutical manufacturing.