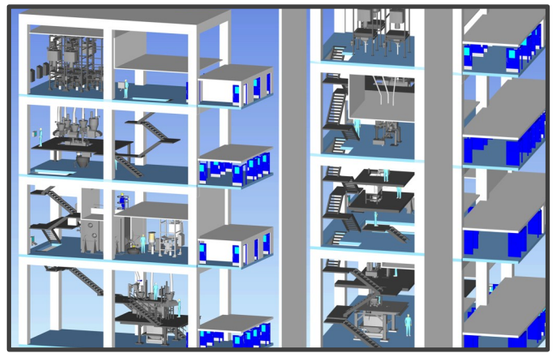
Welcome to our March Newsletter. In this issue we have included a brief introduction to continuous process granulation along with an article on New Product Introduction. For more information on our current projects and to sign up to our email newsletter, please go onto our website www.bpe.ie or contact us directly on info@biopharma.ie.
We do hope you enjoy this newsletter and thank you for your continued support. Any feedback or comments you may have would be highly appreciated.

BioPharma Engineering has recently secured Basis of Design phase works for a new Large Scale Continuous process OSD plant in China. BPE have been engaged to complete the BOD and cost estimate for a new multiproduct large scale OSD plant incorporating continuous granulation processing (wet + dry) with all associated tabletting, capsule filling and finished packaging in a new standalone 50 000 sq. m fully integrated world class facility.

This appointment represents another significant milestone for the BioPharma Team; it marks a major achievement in securing another export driven appointment and in particular our first appointment in China.Our Scope of work for the BOD phase of the project is to complete all process, mechanical, electrical, HVAC & building services & clean utility design activities to BOD phase.

For more details on this project and on how we can assist you in design and project delivering contact John O'Reilly on joreilly@biopharma.ie.



NEW PRODUCT INTRODUCTION (NPI)

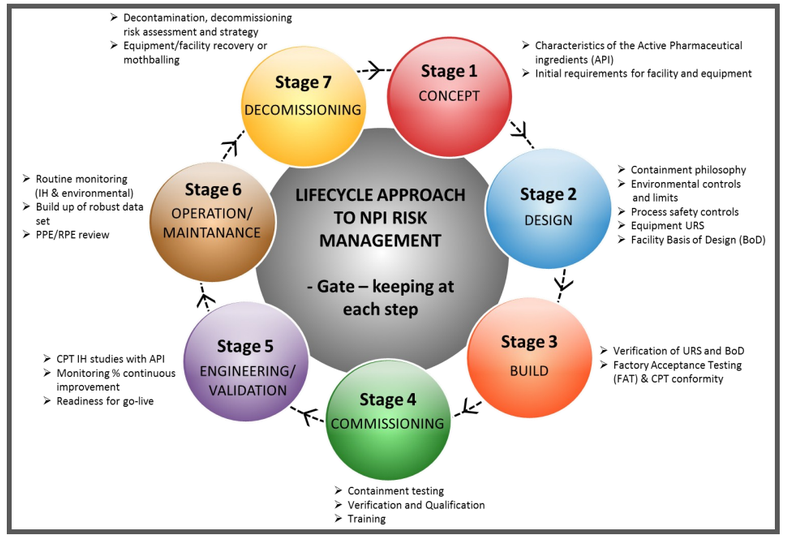
New Product Introduction (NPI) projects are complex and multifaceted. They generally require changes to production methods, equipment, analytical methods, lab equipment, environmental and health and safety systems. New products can be at different phases of development for example Validation, Registration Stability or Early Phase Development and this governs the requirements of the project i.e. Products that are being validated and setup for commercial manufacture will require long term solutions that are robust while products that are in development and require only small quantities need to be cost effective and deliver flexible solutions that are phase appropriate. ICH 7, 8 and 9 requirements need to be met while also achieving the commercial success factors for the product.

Guidance is available from the ISPE Good Practice Guide: Technology Transfer, which is a is a user-friendly manual that presents a clear and concise standardized process for transferring technology between two parties and recommends a minimum base of documentation in support of the transfer request. Another source of guidance is the WHO Technical Report Series, No. 961, 2011.

In Biopharma Engineering, our process engineers have both site and design office NPI experience of over 20 steps of Small Molecule API manufacture across all the stages of a product life. We can facilitate the initial plant / process fit assessments and project scope development of what needs to be completed as well as deliver the capital equipment changes.

New products can require challenging chemistry like Hydrogenations, Brominations and unusual Crystallisation / Isolation techniques. Diverse material handling, safety, containment and environmental solutions for handling raw materials, starting materials, byproducts, intermediates and API material are frequently required.

NPI projects require significant Project Management. Biopharma Engineering can provide experienced Project Management, Scheduling, Cost Control and Project Delivery Systems to supplement a Clients Team, enabling them to focus on the key Process aspects of the project.



For more information contact Mary Collins – Process Engineering Team Lead on mcollins@biopharma.ie.

BRIEF INTRODUCTION TO CONTINUOUS GRANULATION PROCESS

BioPharma Engineering delivered our first Continuous Wet Granulation processing suite for Pfizer in 2008, the suite was designed to produce up to 400kg of product per hour; operate continuously for up to 28 Days between campaigns and was used to continuously formulate up to 4 excipients and 1 API through milling, blending, continuous wet granulation, continuous fluid bed drying feeding into 3000 Litre IBCs for downstream Tableting and Coating.

As mentioned above we are currently working on the BOD phase for a new Continuous Processing Facility which will leverage our previous experience in the delivery of Continuous Wet Granulation with the delivery of 2 large scale wet granulation trains - 400 kg/hr and 1000 kg/hr along with a Continuous Dry Granulation process using Roller Compaction operating at up to 300 kg/hr.

The customised equipment trains detailed above will also be complemented with a number of Off the Shelf fully Continuous Granulation, Tableting and Coating units operating at 100, 150 and 200 kg/hr ranges.

At BioPharma Engineering we have unrivalled practical experience in design, delivery and qualification of Continuous Manufacturing for OSD production. With the right design, Continuous Manufacturing will let you stay ahead of the curve, reduce costs and increase throughput. We have set out a number of challenges and benefits in moving from batch to continuous processing which we would be delighted to discuss with you in further detail:

1. Equipment Selection

Equipment selection is critical to the successful introduction of a Continuous Granulation process. The selection of the equipment is decided by several factors – campaign duration, product throughput, product formulation, solubility and cleaning frequency.

Availability of raw materials and delivery of the materials to the Continuous Suite is another factor to be taken into account in deciding an approach to Continuous Manufacturing. The utilization of Big Bag automated dispensing can dramatically reduce the amount of manual handling associated with traditional batch dispensing and lead to reduced manual handling and labour costs. Availability of raw material in FIBCs may be a challenge in the current supply chain particularly from API suppliers and is an area to be considered early in the move to a Continuous Train.

In addition, a fit with product development / R&D equipment selection may be an important driver for manufacturing equipment selection and needs to be considered in the longer term for new product Introductions. It is crucial in the long term to keep a link between product development and your manufacturing system if you are to attract new products to your site.

2. **Decreased Production Time & Costs**

Removal of the manual interventions associated with batch production will lead to improved product quality due to the removal of batch to batch variation. It will also allow for reduced costs due to increased batch size, less head count to staff the equipment and reduced costs of raw material due to savings incurred in packaging.

Reduction in plant service costs i.e. steam, compressed air, electrical services and cleaning materials in relation to running one processing train versus multiple batch processing trains can also add considerable cost savings to an existing facility.

Improved efficiencies in compression due to increased batch size - where IBC fill capacity can be increased as the granulate is continuously blended and also variability is reduced in the granulate, thus making the follow on step / start up easier.

3. Facility & Capital Costs

Capital costs to construct new solid dosage facilities that incorporate continuous manufacturing systems will be significantly reduced allowing for more effluent of pharmaceutical revenue to be dedicated to shareholder value.

With smaller and more energy efficient buildings requiring less footprint, new facilities will be the less challenging parts of an overall capital expenditure program. New facilities will undoubtedly be leaner and greener when using continuous processing as its manufacturing system.

Current estimates of between 20-35% savings on facility build costs are achievable where a reduced facility footprint is driven by use of relatively small continuous equipment instead of the batch equivalents. In continuous processing, multiple unit operations are directly coupled together. This means that the process has inherent containment attributes, thereby reducing manual material movements and work-in-progress storage requirements.

4. Benefits of Continuous Processing

The decision to adopt continuous processing should ideally be based on process understanding and business requirement. Continuous wet and dry granulation processing may not be a suitable technology when a process relies on back mixing as a control mechanism, or is an inherently slow process.

Several studies have demonstrated the benefits for this type of processing as follows:

- Unattended and lightly attended operations.
- Increased process efficiency with regard to output and yield.
- Reduced manufacturing cost due to low manpower and energy requirements.
- Reduced cycle time due to the inherent inefficiencies of batch processing.
- Reduced space and capital requirements due to the generally small size of continuous process equipment.
- Extension of working hours from 8 hour day to a 24/7 operation.
- Better quality attributes due to improved potential for process control.

For more information contact John O'Reilly on joreily@biopharma.ie.

We would like to welcome the following new team members to BioPharma Engineering

Dermot O'Driscoll – Lead Building Services Engineer

Dermot is a mechanical and building services engineer with more than 20 years experience in the design, construction and commissioning of HVAC and building services systems. He has worked on a wide range of industrial and commercial projects but mainly for the pharmaceutical industry including sterile fill-finish facilities (project engineer with MSD Brinny), API facilities (Eli Lilly and Pfizer) and Oral Solid Dosage facilities (Pfizer Loughbeg). He has had a particular emphasis on energy reduction projects in recent years, including airflow and demand reduction for API and Sterile Fill Finish facilities and CHP projects for both pharmaceutical and food industry clients.

Ben Corbett – Senior Piping Designer

Ben is a senior piping designer with more than 30 years experience in 2D and 3D process and utility piping design including co-ordination, commissioning and construction supervision in API and Bio Pharmaceutical Industry. He has worked on green field and brown field projects for various pharmaceutical plants (Pfizer, Eli Lilly, ROCHE,MSD) amongst others. Ben's vast experience covers all areas of Pharma piping design from high purity bio systems to carbon steel utilities. We believe he will be a valuable member of the team and effective team player with a strong client background and appreciation of site requirements for successful project delivery.

DESIGN MANAGE DELIVER

Our Capabilities

We design, manage & deliver projects for a broad spectrum of clients in the following Industries

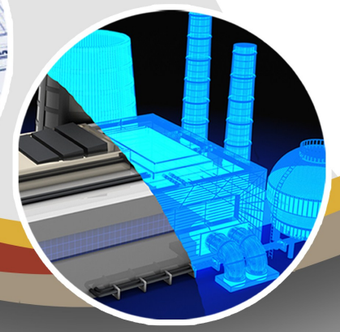
PHARMACEUTICAL

BIOTECHNOLOGY

MEDICAL DEVICES

To find out how we can tailor our service to meet your business goals give us a call or visit our website.

- BioPharma's First China Project
- New Product Introduction (NPI)
- Brief Introduction to Continuous Granulation Process
- New BPE Team Members



BPE BIOPHARMA ENGINEERING

CORK
NSC Campus, Mahon,
Cork, Ireland
T: 021 230 7120
E: info@biopharma.ie

DUBLIN
3013 Lake Drive, Citywest,
Dublin 24, Ireland
T: 01 4693 734
E: info@biopharma.ie

DESIGN MANAGE DELIVER

www.bpe.ie

"Engineering Design & Project Delivery for the Pharmaceutical Industry" | **www.bpe.ie**

BPE BIOPHARMA ENGINEERING