Scale Up of Semisolid dosage forms in Manufacturing Processes

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Introduction

Scale-up is the process of increasing the batch size or a procedure for applying the same process to different output volumes. Preforming scale up in the production processes is a major challenge in pharmaceutical industry.

Quality by Design (QbD) is one of the most used and effective approaches for scale up. Using QbD, pharmaceutical manufacturers ensure the quality of medicines by using statistical, analytical and risk management methodologies in the design, research, development and the manufacturing of the medicines

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A pilot plant can also be defined as the pre-commercial production system which includes new production technology and produces small volumes of new technology-based products.

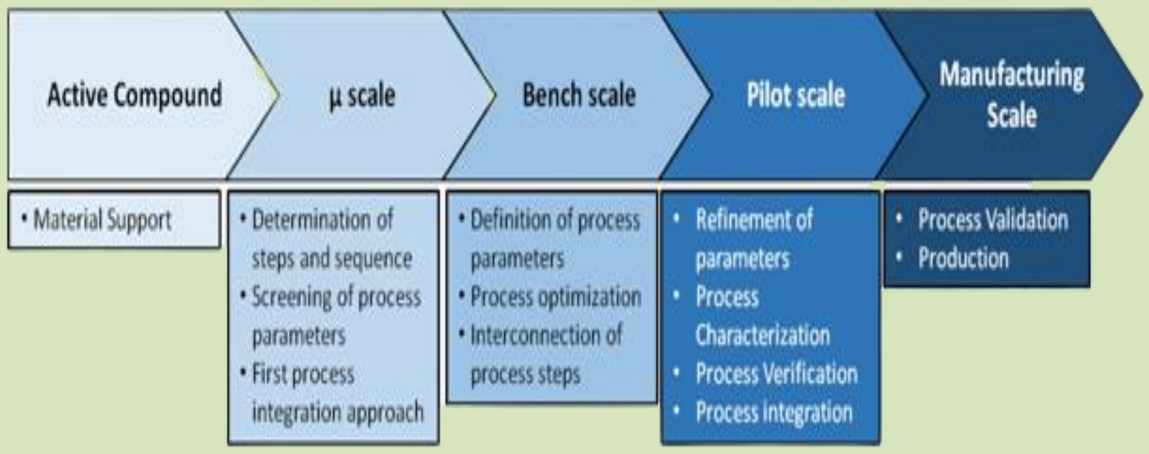

Figure 1: State of the art process of up-scaling

Methods and Materials

For a pilot scale up to be successful a product must be capable of being processed in a large scale often with equipment that only remotely resembles that used in the development laboratory.
The chemical attributes of the product, its quality and efficacy should be maintained after the scale-up even though the production processes is modified as a result of sample size increase and equipment changes.

During the process, Critical Process Parameters (CPPs), Critical Quality Attributes (CQAs) and other important parameters are identified using quality risk tools as Ishikawa diagram and FMEA. Design space should be defined and understood consisting of a set of input ranges (CPPs) that provide high probability that CQAs will meet specification.

And finally, a control strategy needs to be in place to assure that the setting of the process is adequate .

Figure 2: Semi-automatic aluminium tube filling and crimping machine

Figure 3: Optimizing A Perfusion Manufacturing Process

Key points of the scale up

The scale up team should review of a range of relevant processing equipment to determine which would be most compatible with the formulation as well as the most economical, simple, and reliable in producing the product.

Considering this, the chemical attributes of the product are critical, and its quality and efficacy should be maintained even though the production processes are modified as a result of sample size increase and equipment changes.

A well-defined process may fail quality assurance tests in full manufacturing scale even after generating a perfect product in both the laboratory and the pilot plant.

Scale-up of a semi-solid product introduces numerous challenges, mainly related to mixing and creating a uniform, homogeneous material. The product must have the correct viscosity and the desired sensory qualities. The use of different equipment can have a major impact on the final product.

- Robustness of the process
- GMP consideration

Discussion and Conclusion

Using a stepwise and methodical QbD approach during the development and late stage of semi-solid dosage forms will provide a sound and robust platform for process development and will enable the developer to provide a robust control strategy for manufacturing. Using QbD, six sigma tools and experimental design will ensure the manufacturing scale up of semi-solid products is with minimum risk.

All the critical parameters have to be defined and all the risks should be calculated and classified in accordance to their RPN values. The result will be a robust process with satisfying parameters in accordance with the product specification.

Every step along the journey from new drug product concept to commercialization is challenging, but the goal is clear: to mass-produce a product that is exactly the same as the original formulation, regardless of the volume generated.

Figure 4: 10x Production scale-up.
Dumo Turbo DT20 + Melter 10L → Turbo-Mek 200 + Melter 100 (Manufacturer: Marchesini Group)

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