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Short communication

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.

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 (Khar et al., 2013).

Pilot plant scale-up techniques involve reproducible manufacture of an experimental formulation on high-speed production equipment, in a cost-effective manner. The same processes that are used during Research and Development (R&D) of dosage forms are applied to different output volumes; usually 10 times greater than that obtained during R&D (Chanana et al., 2014).

In this article, we will review the key points of preforming scale up in the manufacturing of semi-solid dosage forms.

Materials and methods

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 the ones 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. (Ramasubramaniyan et al., 2014). In order to study relationships and gain information on potential sources of variability, uni/multi variant experiments should be completed, to make sure that the process and measurement capability is understood and defined. Another crucial moment is implementing the quality risk methods and tools as process flow diagram to determine the inputs/outputs that could impact quality (ICH Q10). 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 (Tiwari, 2011).

Key points of the scale up

There are some key points that are critical for scale–up process that need to be taken in consideration when performing scale up process.

First step is close examination of the formula to determine its ability to withstand large scale and process modification. The scale up team should review 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.

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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 (Tiwari et al., 2011).

Robustness of the process

For maintaining and getting a robust process several critical points should be determined in the production process using QRM principles. The critical points like speed of homogenization, time of homogenization, vacuum during cooling of the dosage form, temperature points, contribute to controlling the process and continuous manufacture of product that is in the specification limits. Controlling the critical points in production process can lead to robust and stable process. Experimentation in manufacturing is limited compared to R&D, but the state of robustness can be determined with constant proactive monitoring of the process (Braun, 2021).

GMP consideration

The check list of the GMP items that should be a part of the scale-up should include the following: equipment qualification, process validation, regulatory schedule, preventive maintenance, regular process review and revalidation (Dhobale et al., 2018).

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.

With adequate scale-up protocols taking into consideration the machine performances, the scale up will be done properly.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.

The characteristics of the manufacturing equipment used, including power, speed and size, may influence outcomes significantly.

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. According to FDA's Scale-Up and Post-Approval Changes (SUPAC) guidelines, the entire scale-up process must be validated every time the process is scaled-up by a factor of at least 10.

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