ALTASCIENCES

CASE STUDY

Evaluating Milling Conditions for Scaling Up a Nanosuspension Drug Product

STUDY OVERVIEW

A client contracted Altasciences for our expertise and experience in scaling up the manufacturing of their nanosuspension drug product. Their goal was to have a sufficient quantity of product to support Phase III clinical trials. However, the current manufacturing conditions needed to be optimized to scale up to a 200 L theoretical yield. This study was proposed to best evaluate the milling conditions necessary to constantly and reliably manufacture their nanosuspension product.

STUDY DETAILS

- **Drug Development Phase:** Phase III clinical studies
- **Class of Drug:** Small molecule, BSC Class II
- **Route of Administration:** Oral
- **Equipment:** NETZSCH DeltaVita® 10000 milling system

STUDY PURPOSE

The study aimed to investigate and optimize the milling conditions for the manufacturing process of a drug nanosuspension needed to achieve target particle size at a 200 L theoretical yield through a series of 10 pilot batches. This study was a necessary step to support Phase III clinical studies.

METHODS AND RESULTS

The equipment used for the manufacturing study is the NETZSCH DeltaVita® 10000 milling system, which has a 10 L milling chamber with a motorized agitator and 0.5 mm yttria-stabilized zirconia grinding media. Drug suspension is pumped through the chamber, reducing the drug compound's particle size. As this process is scaled up, the parameters need to be optimized for the increase in drug volume.

Two initial runs were performed to establish the study's baseline process. From this baseline, three milling conditions were evaluated, focusing on two variables: media load and agitator speed. Media load ranged from 88% to 92%, and agitator speed went from 1,000 rpm to 1,100 rpm with the chiller set points at either -5 °C or 5 °C, for a total of 10 runs. The drug compound was milled at a concentration of 25% w/w until the target particle size was reached. The 25% w/w drug nanosuspensions were diluted to 5% w/w, bottled in primary packaging, and placed on stability.

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Once completed, each run was release-tested for appearance, ID, assay, dissolution, particle size, pH, elemental impurities, and resuspendability. Eight of the 10 batches were placed on stability. The stability batches were tested for appearance, particle size, assay, pH, dissolution, and resuspendability. The timepoints were 0, 1, 3, and 6 months. The stability conditions were 25 °C/60% RH and 40 °C RH. Monographs listing acceptable criteria for each of the tests were generated to record the data.

Each batch in the study conformed to the acceptance criteria listed in the monographs. The study paved the way for a smooth scale-up of the nanosuspension by optimizing the milling speed, media load, and temperature to provide a stable nanosuspension for Phase III clinical trials.

CONCLUSION

The pilot batches from this study allowed us to explore and optimize the milling conditions to produce a stable nanosuspension for clinical trials. Altasciences has the unique expertise and experience to take R&D formulations and successfully scale them up for clinical manufacturing.

ABOUT ALTASCIENCES

Altasciences is an integrated drug development solution company offering pharmaceutical and biotechnology companies a proven, flexible approach to preclinical and clinical pharmacology studies, including formulation, manufacturing, and analytical services. For over 25 years, Altasciences has been partnering with sponsors to help support educated, faster, and more complete early drug development decisions. Altasciences' integrated, full-service solutions include preclinical safety testing, clinical pharmacology and proof of concept, bioanalysis, program management, medical writing, biostatistics, and data management, all customizable to specific sponsor requirements. Altasciences helps sponsors get better drugs to the people who need them, faster.