COMPANY INSIGHT

STYL'One, the appropriate tool for QbD in Tableting

Over the last years a distinct trend in the increase in QbD can be observed in the pharmaceutical industry. Do you consider this trend as beneficial for our market?

QbD is at the heart of the development of a tablet formulation. Our customers have been using the results of STYL'One Tableting Instrument to generate data and build their appropriate Design Space for years. Those data have been already included in marketing authorization applications (MAA) in Europe. In April 2017, EMA and US-FDA have agreed on how pharmaceutical firms should **include quality-by-design (QbD) elements in drug approval.**

We are glad to see that EMA and the FDA share common grounds on how those data should be included for new drug application (NDA).

QbD is a simple concept: how to develop a drug product that can be produced in a repeatable manner and cost-effective way. The automotive industry has long been using state-of-the art processes to design cars that exhibit constant and controlled quality and are cost-effective to manufacture. The more conservative pharmaceutical industry has only now adopted such methodology. ICH-Q8 is a great opportunity for the pharmaceutical industry and beneficial for the patients.

> QBD IS AT THE HEART OF THE DEVELOPMENT OF A TABLET FORMULATION.

01 / How can your tableting instrument implement the QbD approach?

STYL'One Tableting Instrument can mimic the exact same process parameters of commercial-size rotary tablet presses. Our customers just have to write a Design-of-Experiments (DOE) with all the process parameters that they think are relevant to the quality attributes of their drug product and consequently identifying the critical ones like CPP (critical process parameter) and CQA (critical quality attribute).

STYL'One has been designed with QbD in mind.

It is a great tool to design robust formulations. We talk about robustness when a drug product can tolerate small variations of process parameters or raw material attributes without impairing the overall specifications of the finished tablet.

> STYL'ONE IS A GREAT TOOL TO DESIGN ROBUST FORMULATIONS.

02 / Why does STYL'One execute studies that are not possible with other lab-scale tablet presses?

First of all small R&D rotary presses cannot mimic the same kinetics than those of large rotary presses. 50rpm on a small turret is not the same as 50rpm on a large turret. That is actually why lab-scale rotary presses cannot reproduce capping in the lab. And Capping is one of the most important issues encountered during scale-up.

But the main drawback of lab-scale rotary presses is that they need a longer set-up and cleaning time, they are less flexible on possible studies and validation and last but not least they require large amounts of powder to run the DOE.

With STYL'One, only 50g per experiment is required to carry-out a full compaction study.

> SHORT EXPERIMENT TIME ENCOURAGES THE RESEARCHER TO EXPLORE NEW TRACKS AND THEORIES.

03 / Which unique attributes or accessories give STYL'One an edge to QbD

Time and the lack of material sparing equipment were critical elements limiting QbD approaches. The STYL'One and its family of instruments overcome these limitations.

If you look at other single sided single punch presses you will detect that they do not possess neither the punch speed nor the forced feeding mechanism allowing to test robustness of critical parameters like the effect of paddle wheels inside rotary tablet press feed shoe. A parameter whose importance can be assessed rapidly with a small amount of powder.

Complex formulations like multilayer or dry coating can generate quality requirements which are not easy to define. The STYL'One tab-in-tab device for example allows for production of small batches with – baldy positioned – cores to determine the criticality of core positioning in the final product quality and helping our customers to define boundaries to set for the precision of production equipment.

Similarly the multilayer software wizard allows customers to define the correct tamping force and weight for each layer with a minimum mass of powder, determining the boundaries of production parameters to ensure layer adhesion and drug load compliance.

04 / Would you have a specific customer example that you can share with us?

One of our customers has used STYL'One to assess the influences of different process parameters of a wet granulation process. With a lab-scale rotary press, the minimum quantity of blend required to run the press was 1kg and their lab-scale high-shear granulator could not produce such large quantity in one batch. Not to mention the huge costs of the API.

With as little as 100g of powder (the tablets were 500mg), they were able to study the influence of the wet granulation process parameters on their CQA (critical quality attributes) as e.g. tablet breaking force, friability, disintegration and dissolution profile and 32 different batches of granules were processed by STYL'One. Their initial Design Space was actually narrowed in order to meet all specifications of the drug product. Those data have been submitted into the marketing authorization application to demonstrate to the medical agency that their process was under control and that any variations have been assessed.

> THE COMPACTIBILITY OF AN API CAN EASILY ASSESSED WITH STYL'ONE TABLETING INSTRUMENT

05 / You keep mentioning process parameters. But how about variability of raw materials, such as API or excipients?

That is in fact another powerful application of the STYL'One Tableting Instrument. Any excipients used in pharmaceutical drug products have to be compliant with pharmacopoeias (USP, European Pharmacopea etc.). However, this compliance is only based on chemical specifications, such as Assay, pH potential hydrogens or impurities to name a few. It is actually possible to test new material attributes (MA) not defined in the monograph. The compactibility of an API can be quantified with STYL'One. One of our customer already implemented a specific quality control test for its API outsourced to a contract manufacturer. Even with API meeting the full chemical specifications, they were actually able to develop a method to pin-point which batches of API were yielding to an out-of-specifications drug product.

I let you imagine the savings they were able to achieve!

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