Materials Characterization in Pharma

R&D spending in the pharmaceutical industry through 2015 was valued at around $58bn as organisations vied to gain a competitive advantage by bringing new drugs to market as quickly as possible[1]. Materials science is now helping pharmaceutical companies to standardize and control areas such as drug form and manufacture to deliver new products more quickly and with greater quality. The pharma industry is increasingly embracing the principles of Quality by Design (QbD) to improve efficiency and ensure good quality and reduced variability throughout the drug production process.

What is QbD?

QbD is defined by The International Conference on Harmonization as "A systematic approach to development that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management." [2]. The FDA's process validation (PV) guidance [3] is also important and adds further clarification, providing a standardised and systematic approach for clinicians, consumers and investors.

The QbD process provides specific Critical Quality Attributes (CQAs) for aspects of drug formulation and performance. A CQA is a physical, chemical, biological, or microbiological property or characteristic that can be measured and maintained within an appropriate limit. CQAs are established to allow for the definition of acceptable variations. Material analysis techniques including dynamic light scattering, gas pyconometry and mercury intrusion are all valuable tools to develop CQAs that ensure acceptable clinical standards. As a drug begins commercial scale production uniformity in manufacture is essential and variation between batches could prove potentially dangerous. Adoption of good materials characterization techniques allow CQAs to be established for both active ingredients (API) and excipients. CQAs can rapidly facilitate the identification of the causes of problems or specific batch deformities.

Particle Size

Particle size is crucial to dissolution rates, bioavailability, and stability and other performance factors in solid and suspension dosage forms [2]. As part of a CQA process, it's vital for manufacturers to explore how particle size affects performance. The Micromeritics NanoPlus HD DLS uses dynamic light scattering (DLS) and photon correlation spectroscopy to analyse particle size in the range of 0.1 nm to 12.3 pm with sample suspension concentrations from 0.00001% to 40%. DLS is also a rapid and cost effective method for measuring the particle by particle surface charge known as zeta potential that controls the stability of suspensions.

Porosity

The properties of a tablet are almost entirely defined by the compaction behaviour of excipients during compression. The tablets tendency to break apart (friability), solidity and dissolution behaviour are all attributes that are linked to porosity. The AutoPore V 9600 uses mercury intrusion to measure the porosity of a tablet and is able to determine a broader pore size distribution of between 0.003 to 1100 micrometers. Process parameters and quality attributes can be achieved for porosity equivalent to a difference of less than 0.1 microliter of mercury allowing a reliable and quantifiable CQA to be established.

Density

Pharmaceutical tablets are manufactured by roller compaction, a mechanised process whereby powders are compressed into a solid dosage form (tablet). The development of accurate density-related CQAs is only made possible by an understanding of the skeletal volume, and the true/apparent density of a mixture.

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The AccuPyc II uses gas density pyncometry to calculate total density and works in tandem with the Dry Flo, solid medium GeoPyc 1365 Energy Density analyser. By combining measurements from the two, instruments users are quickly able to determine skeletal density, envelope density, total pore volume, percent porosity, and closed-·cell pore volume of tablets produced with a variety of press settings.These measurements can then be used to establish solid fraction control parameters as a CQA, which will define optimal settings in the roller compactor for speed, compression and nip angle.

References

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Development, http://www.ich.org/fileadmin/Public Web Site/ICH Products/Guidelines/Quality/Q8 R1/Step4/Q8 R2 Guideline.pdf

3. FDA, Guidance for Industry, Process Validation: General Principles and Practices, Revision 1 -· http://www.fda.gov/downloads/Drugs/.../Guidances/UCMOZOSSe.pdf

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