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New Drug Quality

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QbD is a systematic approach to pharmaceutical development that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management

Quality is of utmost importance in pharmaceutical manufacturing. FDA sets minimum standards, but it is up to industry to exceed these standards and develop high quality medicines. Many recent drug shortages and recalls are linked to issues with drug quality and can be traced back to failures of manufacturer's quality management systems.

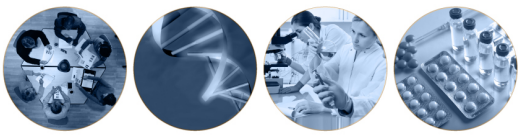
FDA is continuously trying to identify ways to encourage manufacturers to improve manufacturing processes to ensure consistent product quality throughout a product's shelf life. The Agency also works diligently to ensure that manufacturers identify when contamination or other production failures may occur. It is important to recognize that quality cannot be tested into products; it should be built in by design.

Quality by Design (QbD) A sponsor can choose either an empirical approach or a more systematic approach to product development, or a combination of both. Quality by Design (QbD) is a systematic approach to pharmaceutical development that begins with predefined objectives. It emphasizes product and process understanding and process control, based on sound science and quality risk management. This systematic approach can enhance achieving the desired quality of the product and help the Agency to better understand the sponsor's manufacturing strategy. The sponsor can update product and process understanding with the knowledge gained over the product lifecycle. The QbD approach helps to facilitate design of product and process that maximizes the product's efficacy and safety profile, while enhancing product manufacturability. The ICH Q8 (R2) guidance document on Pharmaceutical Development discusses the QbD approach.

QbD can include, for example, incorporation of prior knowledge, results of studies using statistically designed experiments, use of quality risk management, and use of knowledge management (see ICH Q10 guidance document) throughout the lifecycle of the product.

Pharmaceutical development should include, at a minimum, the following:

- Defining the quality target product profile (QTPP) as it relates to quality, safety and efficacy, considering e.g., the route of administration, dosage form, bioavailability, strength, and stability
- Identifying potential critical quality attributes (CQAs) of the drug product, so that those product characteristics having an impact on product quality can be studied and controlled
- Determining the CQAs of the drug substance, excipients, etc., and selecting the type and amount of excipients to deliver drug product of the desired quality
- Selecting an appropriate manufacturing process
- Defining a control strategy



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An enhanced, QbD approach to product development would additionally include the following:

- A systematic evaluation, understanding and refining of the formulation and manufacturing process, including:

- Identifying (e.g., through prior knowledge, experimentation, and risk assessment) the material attributes and process parameters that can have an effect on product CQAs
- Determining the functional relationships that link material attributes and process parameters to product CQAs

- Using the enhanced product and process understanding, in combination with quality risk management, to establish an appropriate control strategy, which can, for example, include a proposal for a design space(s) and/or real-time release testing

Why QbD? The systematic QbD approach can facilitate continual improvement and innovation throughout the product lifecycle.

A greater understanding of the product and its manufacturing process can lead to more flexible regulatory approaches.

The degree of regulatory flexibility depends on the level of relevant scientific knowledge provided in the drug application. The knowledge gained and submitted to the Agency, not the volume of data collected, forms the basis for science- and risk-based submissions and regulatory evaluations. Each application should present appropriate data showing that this knowledge is based on sound scientific principles.

FDA Efforts: FDA is now working on three new areas to support increased manufacturing quality:

1. Continuous processing where materials constantly flow in and out of equipment

2. The use of process analytical technology to monitor and control processes,

3. The development of new statistical approaches to detect changes in process or product quality

Additionally, FDA is incorporating systematic risk based approaches into reviews as industry adopts this approach. FDA encourages the use of novel technologies and innovative analytical approaches to improve product manufacturing and quality. One such effort is a pilot program between FDA and the European Medicines Agency (EMA) that allows for parallel evaluation of relevant development and manufacturing data components of new drug marketing applications submitted to both agencies. Reviewers from both agencies will separately assess the quality/chemistry, manufacturing and control (CMC) section of the new drug applications (NDAs) submitted to the FDA and marketing authorization applications (MAAs) submitted to the EMA. However, both agencies will communicate regularly about the QbD aspects of the applications and work towards harmonizing review approaches.

Never underestimate the importance of drug quality, and always strive to improve manufacturing processes by building quality into products by design.

Until next month,

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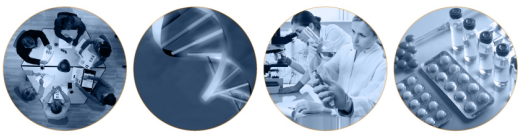

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