WHITE PAPER

# Quality by Design, Every Step of the Way

## An Evolving Landscape: Ensuring Pharmaceutical Quality Through QbD

### Introduction

Since its inception in 2005, Quality by Design (QbD) aims to ensure the quality of medicines by employing statistical, analytical, and risk-management methodology in the design, development, and manufacturing processes of medicines. "QbD was introduced to change the paradigm of pharmaceutical product quality from being product orientated to process orientated," explained Dr. Mansoor Amiji. "Instead of relying on product quality as a readout after the product is made, you start to implement these procedures into the product production processes. This means that in each step along the continuum you are optimizing for quality."

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**Mansoor M. Amiji, PhD**
University Distinguished Professor, Professor of Pharmaceutical Sciences and Professor of Chemical Engineering; Director, Laboratory of Biomaterials and Advanced Nano-Delivery Systems (BANDS) Northeastern University, Boston, MA, USA.

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One of the goals of QbD is to ensure that all sources of variability affecting a process are identified, explained, and managed by appropriate measures so that the finished medicine consistently meets its predefined characteristics from the start of development. The first element of QbD involves identifying the target product profile. This is a prospective summary of the quality characteristics of a drug product that will ideally be achieved to ensure the desired quality, while considering the safety and efficacy of that product.

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Dr. Amiji noted that the first step of this process is to determine whether the product is intended to be administered by oral route, as an injection, or by other routes of administration. Once this has been identified, the specific quality criteria can be ascertained. "For example, if you consider an oral tablet formulation, there are various considerations, such as dosage strength, tablet size, as well as addition of active pharmaceutical ingredient (API) and excipients such as glidants and lubricants, etc. All these processes have to be controlled and optimized to ensure that the final tablet has the appropriate quality assurance and meets the quality requirements of the necessary regulatory agencies," he said.

## Guiding the Process

QbD principles are woven into regulatory guidance documents, primarily the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidances Q8 through to Q11. "These harmonization guidelines help industry understand the necessary requirements in order to develop pharmaceutical products," explained Dr. Amiji. "They inform industrial scientists what is necessary to ensure that their product meets the safety and efficacy requirements to get a product approved in humans. These guidelines are continuously evolving and are common practice across many regions of the world."

With this in mind, industrial-level scientists must be trained appropriately to make sure these guidelines are met. "There is a lot of regulatory oversight into how these processes and products are being developed and companies need to ensure their staff have adequate training so that they are meeting these guidelines. QbD should be carried out by the company developing the product and implemented into each of these processes," said Dr. Amiji.

## An Evolving Process

Since the first product using QbD was developed in 2006, regulatory guidances have continued to evolve based on prior knowledge and it is now standard practice in the pharmaceutical industry to utilize QbD. "There is a lot of precedent in terms of utilization of QbD in existing pharmaceuticals," said Dr. Amiji. "By addressing the processes rather than the end-product, the agencies have become much more streamlined and conscious of cost savings. If you can identify problems during one of the initial processes, you can hopefully solve them before the product is made."

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Due to this continuous evolution of these guidance documents, it is also important that companies keep personnel up to date with any significant changes or developments. "Academic institutions form a vital component of this exercise by producing trained personnel," he said. "However, it is not just the initial training that is important; companies need to implement programs that help workers stay up to speed with developments and continue their training."

For some products, such as first-in-class drugs, implementing QbD is slightly more complex. "If you are the first company to develop a product that has not been made in the past, for example a nanoparticle-based drug delivery system, the FDA needs to have much greater oversight in ensuring that QbD is implemented correctly," explained Dr. Amiji. "In those scenarios, there will be constant dialogue with the regulatory authority in order to ensure the product meets the appropriate quality requirements. We saw an example of this with the COVID-19 mRNA vaccine – the quality assurance was very different to some of the traditional vaccines that were developed, such as those using recombinant technology or attenuated viruses. Each case mandates its own quality assurance matrix."

Regardless of whether a company is producing a product for the masses or for select individuals, Dr. Amiji notes that QbD is always a key quality requirement. "In terms of personalization of medicine, some of the attributes would need to be refined appropriately for the product, because each of product will dictate specific quality criterion. Ultimately, the tests that are necessary will differ depending on the product, but quality assurance will always have to be in place to ensure that any product developed is safe and effective."

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Dr. Amiji concluded that over the past decade, a lot of effort has been put into the successful implementation of pharmaceutical QbD. "In the past, if a product did not meet quality requirements it would have to be discarded, which would have significant financial implications and waste a lot of time and resources. QbD has therefore been a well-received and successful program and almost all companies producing pharmaceutical products now have to meet these requirements," he said.

### About Mansoor M. Amiji, PhD

Dr. Amiji received his undergraduate degree in pharmacy from Northeastern University in 1988 and his PhD in pharmaceutics from Purdue University in 1992. Over the years, his research has received over $40m in sustained extramural funding from the National Institutes of Health (NIH), National Science Foundation (NSF), foundations, and biotech/pharma industries.

Dr. Amiji has supervised research efforts of over 120 post-doctoral associates and graduate students. He has also edited 10 books, along with over 70 published book chapters and over 360 peer-reviewed articles.

Dr. Amiji has received several awards including the 2006 NSTI Award for Outstanding Contributions towards the Advancement of Nanotechnology, Microtechnology, and Biotechnology, and the 2007 American Association of Pharmaceutical Scientist's (AAPS) Meritorious Manuscript Award. He is a Fellow of both AAPS and the Controlled Release Society. He has also received the Distinguished Alumni Awards from both Northeastern University School of Pharmacy and Purdue University College of Pharmacy.

**PerkinElmer, Inc.**
940 Winter Street
Waltham, MA 02451 USA
P: (800) 762-4000 or
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**www.perkinelmer.com**

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