Applying Quality by Design to Pharmaceutical Research and Development

By Shawn Watson,
Head of Research and Development at Pharmaceutics International, Inc (Pii).

The origins of pharmaceutical Quality by Design (QbD) can arguably be traced back to W. Edwards Deming's book, Out of Crisis, first published in 1982. In the book, Deming introduced his fourteen points of management which have had a significant impact on how organizations pursue intended outcomes. Deming's third point transformed how we achieve quality; not through a reliance on post-manufacturing testing, but by designing quality into products from the initial stages of development.

The FDA's guidance concerning QbD began taking shape not long after I began working as a bench chemist, the first role I had in the pharmaceutical industry. QbD has always been a part of my professional life and I hold a strong belief that it begins in the early stages of drug development. It has also been continuously refined by FDA in coordination with industry and my own understanding has been continuously advanced through experience.

Pharmaceutical QbD

The concept of QbD asserts that quality be designed into a drug based on an understanding of the product and the process by which it is developed and manufactured. QbD is often discussed in the context of process development and manufacturing. However, this article focuses on how QbD is applied to research and development (R&D) to drive better results throughout the drug development process.

Much of the work applying QbD to R&D is dedicated to understanding the drug product under development and includes gathering and organizing data. The drug development process from concept to an initial clinical batch generates a significant amount of data and this data must be effectively managed over time across a number of functional disciplines.

The data-rich environment created when applying QbD to pharmaceutical R&D demands a knowledge management system with three key components: reliable databases, reporting systems that support decision-making, and sound scientific observations. Let's look at each of these a bit more detail.

Reliable Databases

Successful drug development requires a lot of resources, arguably data is one of the most essential. The importance of databases demands that it be reliable, but what constitutes a reliable database? For me reliable databases have two key features: integrity and completeness.

Data integrity is a topic of great interest across the pharmaceutical industry and volumes have been written about it. Over the past twenty years, our ability to use data for better results has improved and so has the importance of its integrity. To address compliance with cGMP the FDA issued final guidance for data integrity in 2016. This is not intended to be a paper on data integrity, however, we create gigabytes of data over the lifecycle of a drug product. This data must be accurate, and I will simply state that ensuring data integrity is a leadership function.

Completeness of databases means that there must be enough of the right data to advance development, but not so much that resources are unnecessarily expended on directionless experiments. Database completeness requires a quality target product profile (QTTP) completed as early as possible with well-defined critical quality attributes (CQA). For example, a product uniformity issue may be discovered early that will prevent scale-up if variability cannot be reduced. The lack of complete data could delay, or even prevent, a necessary solution to support scale-up.

Informative Reports to Support Decision-Making

There are two key components for reporting data to support effective decision-making to advance drug development--understandable reports and the presence of decision-makers.

Reporting scientific data varies by organization and development project, and there are many good technology-solutions available. I recommend that R&D organizations be intentional in the platforms they choose to support their efforts. Well-intentioned efforts to either empower each scientist with separate procedures of their choosing or to create efficiencies with overly standardized reporting have each led to dysfunction. R&D leaders must balance the need for standardized reporting with supporting the scientific process. To help achieve this balance it is important to understand what decision-makers need and let that drive the reporting.

Having the decision-maker present seems obvious, but I have sat through many meetings that presented valuable data intended to help advance a decision without the presence of a decision-maker. First let's define decision-making authority. A decision-maker is one or more people who have the authority to allocate resources and establish or modify priorities to take the next steps to advance a drug development project. The presence of a decision-maker is an imperative that flattens the decision-making organization, creates efficiency, and greatly reduces delays.

I stated that the decision-maker could be more than one person. Collaborative decision-making is common and therefore it becomes important to present data to the collective decision-making body. Also, I am head of R&D for a contract development and manufacturing organization (CDMO) that provides services for clients. Our service model is one that is collaborative and transparent, and it is essential to include the client's decision-making in our efforts.

Enabling Scientific Observations

Being able to provide meaning to the observations of R&D scientists is challenging and is where the art of drug development plays a prominent role. There are no statistical models that help us trend scientific observations and efforts to quantify scientific observations often fall short. For example, can you really standardize the way a scientist describes how a tablet disintegrates in a dissolution basket? And if you could, would you want to?

At the heart of QbD is the ability to study critical material attributes (CMA) and critical process parameters (CPP) to form critical quality attributes (CQA). This level of discernment requires experienced scientists who are confident in making critical judgment calls. The scientists making these calls must understand the intended finished product specifications, the ultimate therapeutic purpose of the drug, and the patients for whom it is intended.

An R&D organization that effectively applies QbD requires a distinctive leadership approach and organizational culture that can articulate intended outcomes and then give the team the flexibility and space to pursue those outcomes. Nothing demonstrates the modern knowledge-based workforce more than a pharmaceutical R&D team working the way I've described.

QbD begins at the R&D stage of drug development and requires advanced knowledge management capabilities with three key components: reliable data, clear reporting that supports decision-making, and a team of experienced scientists who exercise judgment to achieve intended outcomes. QbD-based R&D like I've described can help streamline the drug development process to avoid delays and deliver better results faster to patients.

Shawn Watson is responsible for all product development, including sterile, non-sterile, oral, and topical dosage forms, as well as analytical methods development at Pii. He has over twenty years of leadership experience in the pharmaceutical industry in specialty, generic and contract development and manufacturing organizations (CDMOs). His wealth of knowledge spans Research and Development, Quality, and Technical Services.

Prior to joining Pii, Shawn served as the Vice President of Quality and Laboratory Operations at Lupin Pharmaceuticals, Vice President of Compliance at Sigmapharm Laboratories, and Supervisor of Analytical R&D at Teva Pharmaceuticals. Additionally, he has held a variety of other key positions including Vice President of Quality, Senior Director of Chemistry & Manufacturing services, and Senior Manager of Analytical Research and Development. Shawn's passion for working in the pharmaceutical industry began with his very first job as a quality control chemist with a CDMO and included work with Pii. Shawn earned a Masters of Business Administration from the Fox School of Business at Temple University, a Masters of Science in Chemistry from Villanova University, and a Bachelors of Science in Chemistry and Biology from Heidelberg University. He also obtained a six sigma green belt from Villanova University.

About Pii

Pharmaceutics International, Inc. (Pii) is a contract development and manufacturing organization (CDMO) with a passion for solving problems efficiently with the highest quality standards.

Pii's Hunt Valley, Maryland campus includes 70 manufacturing suites with 4 integrated aseptic filling lines delivering quality, safety, and efficiency. Our professionals have extensive experience with small and large molecule compounds, developing and manufacturing complex parenteral drugs, extended-release formulations, non-aqueous injectable drug products, and lyophilization. Learn more at https://www.pharm-int.com/