

Annex to Q8: Quality by Design in Product Development

By John Avellanet, Managing Director and Principal of [Cerulean Associates LLC](#)

Reprinted with permission from SMARTERCOMPLIANCE™ 2(1): p 1,4-5 (January 2008)

The International Conference on Harmonization (ICH) has published its draft “Annex to Q8 on Pharmaceutical Development.”

The draft document details the expectations of Quality by Design in the preclinical product development arena.

Beyond Pharmaceuticals

A note of caution: assuming that Quality by Design as outlined in the Annex applies only to new drug development is akin to assuming the US Food and Drug Administration (FDA) only regulates food and drugs.

Today’s reality is that ICH standards are applied across the medicinal spectrum, from pharmaceutical firms to biotechnology businesses and medical device companies.

How are you preparing to incorporate the principles of Quality by Design into your new product development?

Regulatory Flexibility

The top reason advocates of Quality by Design (QbD) often cite for adoption is the ability to receive more flexible treatment by regulators and investigators. For critics of Quality by Design, this flexibility—if present at all—is far too little, too late.

Our experience shows that while the final degree of regulatory relief is still up in the air, a number of Quality by Design activities do result in significant business advantages that translate into compliance flexibility. Two of these tactics are highlighted in the draft Annex to Q8.

Patients' Needs

The first QbD activity is understanding the needs of your product's intended patients (and healthcare providers).

The degree of regulatory flexibility is based on the relevant scientific knowledge gained and submitted to regulatory authorities. And while the Annex (and other guidance documents) describes clear, one-to-one relationships to laboratory and clinical items (dosage form, stability, etc.), what is often overlooked is how those exact same items directly relate to patient needs. It may be in the biopharmaceutical company's interests to have the dosage form and route be intravenous, but is it in the patients' interests?

The validity of patient needs and wants must be based on sound scientific principles as well, but not those taught in analytical chemistry or nanotechnology engineering.

Rather, the science of patient needs assessment is the science of consumer requirements gathering, analyzing and incorporating into new product development. Long time practitioners include industries such as telecommunications, computer software, automobile engineering, and consumer products like running shoes and toothpaste.

One of the key challenges to QbD product development success is a lack of cross-functional involvement early in the process. A way to deepen your firm's knowledge of the new product—and demonstrate to regulatory authorities the degree of your expertise—is to involve marketing, sales and finance departments at stages along the product development process; if your firm makes a medical device reliant upon computer technology, an IT representative may also be of value.

Marketing personnel can use any of the methods available today—virtual customers, focus groups, etc.—to reduce your risks by capturing patients' needs; this then will help you draw direct linkages to the unique aspects of your product.

Valid collection and documentation of patient needs will also help you when seeking reimbursement from insurers and government agencies (e.g., Medicare).

Design Space

To effectively implement Quality by Design and achieve regulatory and quality systems flexibility, you need to understand the concept of design space as applicable to your business model.

Confusion continues to reign in the industry as to the meaning and extent of "design space," but the Annex to Q8 will help clarify the role of design space in transferring a new product design into final product manufacturing.

In essence, design space allows you to carve out a virtual range of characteristics for any item in your manufacturing process (raw materials, temperature, speed, etc.), and as long as you

have demonstrated through the product development process that your final product is not harmed by changes within those ranges, you are free to make changes inside the “design space.”

Seen in this light, design space is part of your control strategy for consistently producing a safe, efficacious, quality product while providing you operational flexibility.

Design space also plays a key role in demonstrating your ability to increase your product knowledge and demonstrate continual improvement. In turn, these two aspects of design space will lower your costs over time, reduce your risks and help improve your ability to fend off patent and intellectual property challenges.

Done well, continual improvement in design space will lead to new innovations, new patents and new revenue opportunities.

Final Thoughts

When I give workshops at various biopharmaceutical companies on Quality by Design and applying it to their specific situations, one question I am often asked is: will Quality by Design improve our new product development success rate (in addition to speeding time to market)?

My own experiences as well as those of my clients allow me to say “yes” and then I usually qualify that answer: given the Life Sciences’ recent adoption of QbD, when it comes to improving success rates for all new products to make it through preclinical, clinical and marketplace approvals, there is simply not enough data to answer this question conclusively.

However, parallels to the automobile industry (see my *BioProcess International* article, “Lessons from the Auto Industry”) as well as medical devices (see my case study, “Using Quality by Design to Define Your Preclinical Package,” in the *European BioPharmaceutical Review*) can be drawn.

In those contexts, the principles of QbD, when properly applied, have provided improved rates of success if only because new product concepts and prototypes that are ultimately unsuitable are easier to identify earlier in the development lifecycle.

Executives wanting to incorporate QbD into their new product development process need to be realistic as to their goals. With the right mindset, executives (and their companies, shareholders and patients) can benefit from a good Quality by Design-based new product development program.

Are you ready?

About the Author

John Avellanet is a former *Fortune 50* subsidiary C-level medical device and biotechnology executive where he created, developed and ran his firm's Records Management and IT departments. In 2006, he founded his independent consulting firm, Cerulean Associates LLC (www.ceruleanllc.com) and has since become one of the leading experts on Quality by Design.