The regulatory concept of Quality by Design is a gateway to improved cost control and faster, bigger returns on investment. This article discusses how pharmaceutical manufacturers can unlock these benefits by using a system that integrates their product development and regulatory sciences and submissions teams, focusing on quality at every step.

Depending on who you ask, the emergence of Quality by Design (QbD) principles in the pharmaceutical regulatory landscape heralds either unwelcome new challenges for drug developers or a golden opportunity to improve quality and drive better business outcomes.

Neither opinion is objectively wrong. Traditionally, generics manufacturers could submit an Abbreviated New Drug Approval (ANDA) on the grounds of an off-patent drug’s historic success, using publicly avail-
Integrated product development and regulatory submissions stage gate system, which I'll refer to as a stage gate system, or SGS, throughout this article. An SGS should offer you and your team a detailed roadmap to get from project initiation to post-approval commercial manufacturing, no matter your dosage form.

**Features of a robust stage gate system**

Whether you plan to develop your own SGS or turn to an experienced partner to implement a system, knowing how to recognize a well-planned SGS will serve you well. Here’s what to look for:

- **Quality is its core principle.** If QbD is the objective, then your SGS should be the playbook that shows you how to get there. The SGS that I’ve developed has six main stages, as shown in Figure 1, but that number can vary. What matters is the way your SGS champions quality from early feasibility discussions all the way to commercial process validation. It should define the roles, deliverables, and expected outcomes involved in each stage of your product development and regulatory submission process. This gives you the benchmarks you need not only to assess and report on the quality attributes of your product, but to understand and improve the processes that shuttle the product through its R&D and commercial lifecycle. This is how quality gets done.

- **It’s designed to keep you nimble.** As you progress through development, optimization, scale-up, transfer, and validation of your drug products, you need both control strategies to ensure ongoing consistency and flexibility to adapt to emerging opportunities to cut costs and improve quality. A strong SGS gives you both, balancing careful management strategies with the agility to accommodate shifting variables such as product complexity, API availability, and evolutions in technology.

- **It embraces collaboration.** One of the key ways a well-executed SGS achieves QbD is in rethinking how able data to demonstrate the safety and efficacy of the final product. In a post-QbD world, however, the final product’s quality isn’t enough to win approval; regulators want to see data-driven risk management practices designed into every element of the drug development process, from project initiation through commercialization. This challenges manufacturers to change the way they’ve always done things and embrace transparency and data-driven discovery.

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For companies that successfully adapt, the potential rewards of QbD are huge, long-lasting, and extend well beyond the obvious goal of regulatory approval. QbD principles can lead to improved cost control because you’ll know your process inside and out and will be able to find leaks in your spending. You’ll also be well-positioned for rapid regulatory approval, increasing speed to market. Finally, you’ll increase return on investment because you’ll have systems in place to easily manage post-approval changes and ensure the quality and sustainability of your commercial process.

Unlocking these rewards takes a flexible and modern strategy that harmonizes two critical elements of success: how you make your product, and how you prepare your regulatory documentation. I call this strategy an integrated product development and regulatory submissions stage gate system, which I’ll refer to as a stage gate system, or SGS, throughout this article. An SGS should offer you and your team a detailed roadmap to get from project initiation to post-approval commercial manufacturing, no matter your dosage form.

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**Figure 1**

Sample product development and regulatory submission stage gate system
R&D and regulatory sciences and submissions (RS) teams work, primarily by ensuring that they work together. It updates more traditional relay-based workflows, in which an R&D team might “hand off” information like a baton to the RS team. Instead, a workflow driven by SGS and based on QbD principles sees both teams working closely together from the start, with knowledge transfer included as a natural feature of the product development lifecycle.

How a stage gate system can improve your regulatory and commercial success

An SGS prioritizes everything that matters to a generics OSD manufacturer—cost savings, speed, flexibility, and quality—and eliminates or minimizes all of the redundancies and vulnerabilities that get in the way of those objectives. The result isn’t just about bringing a product to market, it’s about developing a holistic and harmonized drug development and regulatory submissions program that will pay dividends on every new investigational project. This is what you can expect:

Your ROI will be higher, and you’ll get to it sooner. For drug product manufacturers, ROI is a question of speed. The faster and less onerous the regulatory approval process, the sooner a drug product graduates from the costly development pipeline into the commercial marketplace, flipping a project from red to black.

That’s why a good SGS engages the RS team from the start, putting them in the foxhole alongside R&D so they can proactively translate scientific data into real-time, evidence-based documentation at each stage gate. By the time a product reaches a late stage, such as the bio-batch manufacturing that immediately precedes the final documentation step, the RS team is already well on their way to completing their full FDA submission. Not only that, they’ve likely accrued more science-based evidence than the regulations require, giving the FDA a meticulous and comprehensive argument in favor of swift approval and preventing or reducing further delays caused by post-approval changes.

You’ll eliminate costly knowledge gaps between teams. Risk thrives in the gaps between fragmented teams. If your R&D and RS teams aren’t integrated, you risk lost time while they manually exchange, translate, and update information, and quality may backslide as data is pushed and pulled from one team to the other.

Your SGS will introduce a leaner, more streamlined process that integrates disparate roles and responsibilities, eliminating these knowledge gaps and protecting the integrity of source data.

You’ll have improved cost control and minimal downtime. Historic approaches to drug product approval hinged on the product’s final release. How the product got there was more or less extraneous to the regulatory outcome.

QbD works differently. It seeks to examine your drug production process down to its elemental parts, so that every variable that could potentially impact your product’s quality in its journey to final release is uncovered, understood, and optimized. This matters to regulators with a QbD agenda, and it should matter to manufacturers who want to control their bottom lines while maintaining the trust and loyalty of their end consumers.

An SGS is an invaluable tool in this pursuit. It provides a framework for multivariate experimentation, which gives manufacturers real-time feedback on their batch-to-batch quality and consistency. This opens a vital window of opportunity for correcting deviations before it’s too late, which dramatically reduces the risk of manufacturing downtime. The result is a healthier balance sheet and a better product.

When challenges arise, you’ll adapt quickly and cost-effectively. Even with the most robust SGS at your service, challenges happen. Safety signals precipitate protocol amendments, turbulence in the API marketplace means switching to a new supplier, emerging technology offers you a new opportunity to stay competitive—anything is possible, and every drug development and regulatory submissions process will need to navigate unforeseen change to some degree.

Your SGS is designed for these moments. It provides the framework for developing very well-understood and meticulously documented processes, which comes with a big benefit: when you understand your process inside and out, you know how to modify it without impacting your final product’s quality. There are no mysteries or unexplored variables to throw production off track. And because you have the same integrated team working together on both your product-development activities and your submission paperwork, you can accommodate change with only minor updates to your required regulatory documentation.
A big impact on quality and the bottom line

As the principles of QbD increasingly permeate the pharmaceutical industry, manufacturers are well advised to embrace an SGS. Not only does a well-executed SGS position a drug developer for smoother, faster regulatory approval, it also creates opportunities for improved financial outcomes overall, driven by the principles of evidence-based process control and end-to-end team integration. Whether you develop your own SGS or find an experienced partner to design and operationalize one to suit your needs, this could be the most impactful and profitable adaptation you make for years to come.

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