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Quality First: How to Reduce the Risks Created by Next Gen Biologics

A new quality-focused mindset is required to create robust risk management systems that add value for the organization, address distribution challenges and generate better patient outcomes.

The pharmaceutical industry is changing dramatically. While the blockbuster drugs of the 1990s such as Lipitor® continue to play an important role in managing patient illnesses, industry focus is now shifting to delicate therapeutic products such as large molecule biologics and new molecular entities (NMEs), including innovative cell and gene therapies (CGTs).

Biologics present significant challenges though; all are costly, complex to manufacture, in limited supply, usually temperature-sensitive with a short shelf life and are often designed to treat small, geographically-dispersed populations suffering from rare or ultra-rare conditions.

52%

The amount biologics are expected to contribute to the top 100 product sales[1]

The Growing Demand for Specialty Logistics

Managing such challenges has led to significant changes in the way a growing portion of pharmaceutical products are now handled, with the industry increasingly turning to high-quality specialty logistics solutions that can manage:

- Rigorous transportation and storage requirements
- Ever-increasing supply chain complexity
- Growing regulatory oversight at local/international levels
- Precise delivery windows
- Increased data/security requirements

But what do modern logistics challenges actually look like? Consider these two real-life examples:

Individual Therapies

Kymriah is a genetically modified autologous T-cell immunotherapy for treating acute lymphoblastic leukemia. Each dose of Kymriah is created from the patient's own T-cells with the final product shipped in liquid nitrogen shippers at -120°C or lower.[2]

Nationwide Programs

India's immunization program serves 27 million infants and 30 million pregnant women each year[3]. However, a 2012 study found that up to 36% of test shipments containing 2-8°C vaccines were exposed to subzero temperatures while up to 66% were subjected to temperatures greater than 8°C[4] — failures that would significantly compromise product stability and potency.

As the above examples demonstrate, the impact of even a hypothetical 1°C temperature excursion outside specification on a high-value shipment can have a huge impact on stakeholders and patients. For instance:

QA Personnel

Output and productivity decreases as they investigate the excursion; the 'due diligence' required may cost upwards of $10,000 per excursion — whether or not the product is ultimately deemed usable.

Manufacturing

Accommodating an unscheduled production run requires a shift in focus and a reallocation of resources. Sourcing of APIs, unanticipated equipment change-overs and reorganization of the production schedule will likely come at a premium.

Sponsor/Pharmaceutical Company

The impact of a major product loss can be devastating, both financially and socially. In clinical trial applications for example, it can lead to study delays, loss of patients, compromised retention rates, delayed regulatory approvals, and loss of confidence by investigators, clinical staff and patients.

Patients

Missing a scheduled dosing can exacerbate a patient's symptoms, subject them to unnecessary stress and further compromise their condition.

Counting the Cost of Failure & Quality

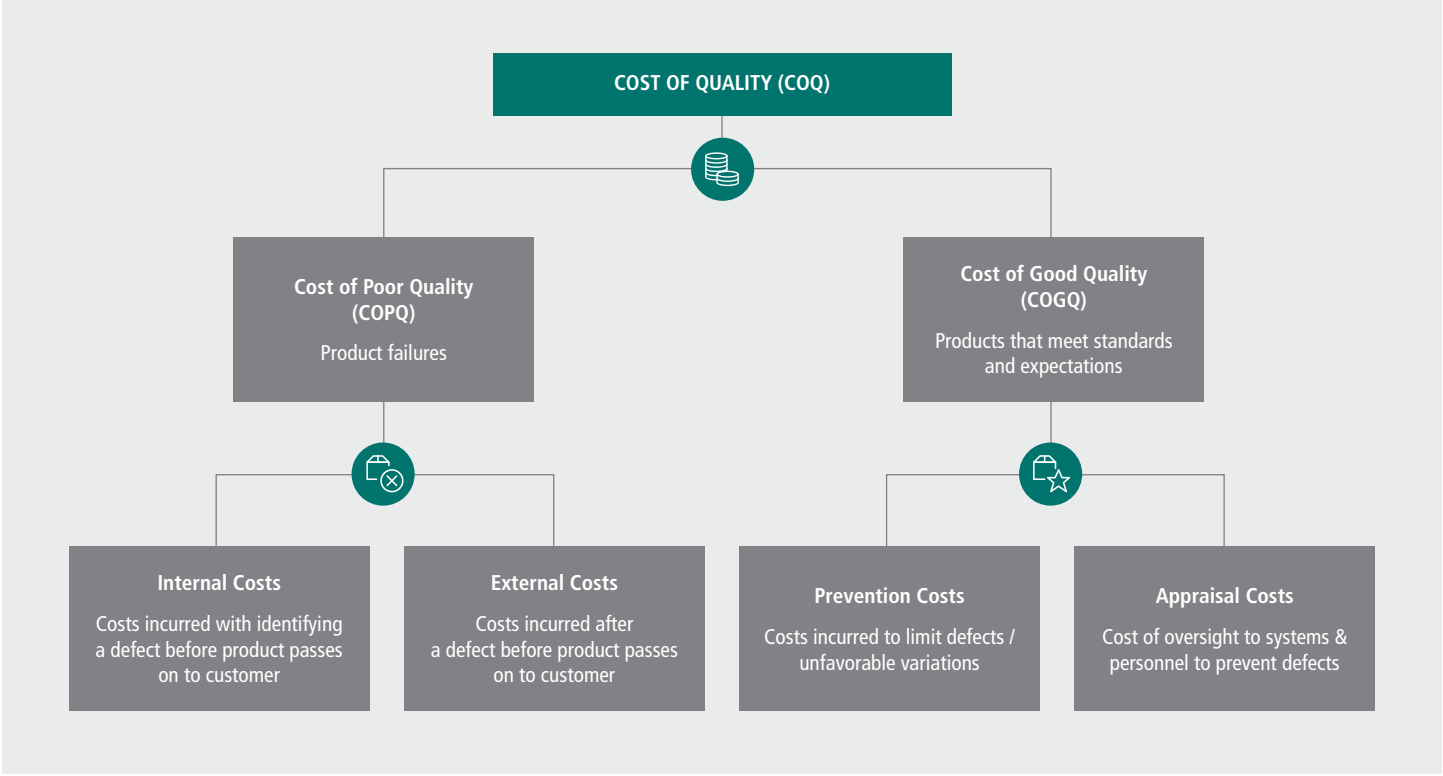
So what is the actual cost of a 1°C out-of-spec temperature excursion? In the worst case scenario — a temperature failure that results in total product loss — the numbers are staggering, with some industry analysts setting the total 2014 annual loss at approximately $35 billion[5].

Key elements identified include lost product costs ($15.2 billion), root cause analysis ($8.6 billion), clinical trial loss ($5.65 billion), replacement costs ($3.65 billion) and wasted logistics costs ($1 billion). Such figures though, do not include the intangible costs such as the negative impact on patients; loss of reputation, credibility and goodwill; loss of revenue and reduced profitability and more.

It means a risk management strategy and decision-making tree must be created that ensures quality while managing costs. Part of the answer lies in understanding the true Cost of Quality (CoQ) in terms of manufacturing and how its methods and practices should be adopted in distribution.

COQ in Manufacturing

The Cost of Quality is typically defined by a product that meets quality expectations and a product that does not. In manufacturing, the COQ is divided into two categories — Prevention and Appraisal — while the Cost of Poor Quality is segmented into Internal Costs and External Costs:



COQ in Distribution

Although designed for manufacturing, these categorizations are equally viable in distribution where the costs of failure can be attributed to either:

Internal Costs: Product/productivity loss, QA, replacement costs, return and destruction.

External Costs: Patient impact, study/product delivery delays, re-recruitment, reputation/credibility and litigation.

In distribution, both the prevention and appraisal costs of COQ should include the cost of identifying and selecting the third-party logistics providers who are able to meet on-time and in-spec delivery expectations:

Prevention Costs: Capability assessments of logistics providers including QMS/compliance, facilities, packaging capabilities, reliability, on-time delivery rates, geographic scope, IT/data management capabilities, accreditation, training, experience, reputation and incremental service costs for specified products/lanes.

Appraisal Costs: Supplier assessments, quality audits and local inspections.

It's worth considering too that the incremental logistics costs will never outweigh the costs associated with a significant high-value product loss generated during distribution.

Why Distribution Must Evolve

Most quality innovation in the pharmaceutical industry over the past decade has originated on the manufacturing side of the business, but today's pharmaceutical shipper will undoubtedly appreciate that quality does not stop at the factory door. In the real world, true quality is only achieved when the right patient receives the right drug, at the right time and in the right condition, underscoring the significance of post-manufacturing delivery as a critical part of both the supply chain and the quality equation.

It is now critical to recognize transport and logistics as an extension of manufacturing activities that must be subject to the same standards, scrutiny and oversight. Indeed, they should be included in the overall risk assessment determined at the beginning of the process as part of an all-encompassing manufacturing/distribution protocol.

Face the Future

In today's world the high cost and complexity of large molecule therapies, tightening bottom lines and intense competition have left no room for error in either product development or distribution — and with the global pharmaceutical cold chain expected to reach $16 billion by 2020, the focus on quality will and must continue to grow.

As an industry, we can no longer afford to be wrong; the errors are too costly and the fallout too far-reaching — especially for patients who rely on us all, day in, day out.

Take the Next Step

Discover how to successfully navigate the many manufacturing and distribution challenges of next generation biologics by:

- Identifying the true Cost of Quality — and Failure
- Understanding the impact of inefficient supply chains
- Analyzing the critical benefits of next gen logistics
- Uncovering vital insights through in-depth case studies.

To learn more, download World Courier's white paper: 'The Cost of Quality in the Specialty Pharmaceutical Supply Chain'

Endnotes

[1] Most quality innovation in the pharmaceutical industry over "World Preview 2017, Outlook to 2022", EvaluatePharma®, 10th Edition, June 2017, page 6.

[2] "FDA approval brings first gene therapy to the United States", FDA News Release, August 30, 2017.

[3] Tiwari R et al,"A study to assess vaccine wastage in an immunization clinic of tertiary care centre, Gwalior, Madhya Pradesh, India", International Journal of Research in Medical Sciences, June 2017.

[4] Murhekar, Manoj V., et al, "Frequent exposure to suboptimal temperatures in vaccine cold-chain system in India: results of temperature monitoring in 10 states", World Health Organization Bulletin, 2013 Dec 1; 91(12): 906-913, Published online 2013 Sep 9. doi: 10.2471/BLT.13.119974.

[5] "Cold Chain Shipping Loss in Pharmaceuticals", CargoSense, http://www.cargosense.com/cold-chain-shipping-loss-in-pharmaceuticals.html.