

New CMC Submission Approach Needed to Foster Transparency and Continuous Improvement, PhRMA Team Says; Embedding Control Strategy as Regulatory Commitment in QOS Proposed

A working group of prominent CMC experts across the member companies of the Pharmaceutical Research and Manufacturers of America (PhRMA) has formulated a proposal for a more performance and risk-based regulatory approach to CMC submissions that would better accommodate post-approval manufacturing and control improvements.

The proposal is emerging from an intensive review by a PhRMA Limited Duration Key Issues Team (LDKIT) focused on the problems in the current CMC review paradigm that have prevented industry's quality by design (QbD) efforts from achieving the promise of regulatory flexibility throughout the product life-cycle.

Pharma's LDKITs are set up under its Technical Development and Operations Committee (TDOC) to explore particular front-burner regulatory issues and develop a consensus proposal for addressing them.

The CMC process LDKIT has honed in on the problems with the structure, content and function of the marketing application itself as needing to be addressed to reach a more continuous improvement-based manufacturing paradigm.

The key to improving the review process, the team maintains, is building a "comprehensive" control strategy into the quality overall summary (QOS) that will define the regulatory commitment and determine, in turn, how the post-approval CMC regulatory oversight is handled.

PhRMA Proposal Aired at PQRI Conference

The PhRMA LDKIT took the occasion of a conference cosponsored by the Product Quality Research Institute (PQRI) and FDA in mid-September in Bethesda, Maryland to outline the proposal in anticipation of having the full proposal ready to present to FDA this fall.

The team's thinking was explained by Pfizer Global CMC VP Roger Nosal at a session focused on the "current practice and future directions [of] life cycle management and post-approval changes."

Nosal delved into the problems that the current CMC filing approach create for both industry and FDA and the benefits that would flow from evolving it along more risk and performance-based lines. *[Nosal's complete remarks are provided in the full IPQ story.]*

[Story continues on the following page.]

PhRMA LDKIT Members

Member	Company	Member	Company
Dan Bollinger	Takeda	John Lepore	Merck
Xavier Castell	Takeda	Rick Lit	Amgen
Andrew Chang	Novo Nordisk	Steve Mason	Amgen
Graham Cook	Pfizer	Moheb Nasr	GSK
Frank Diana	Endo	Roger Nosal	Pfizer
Jeff Ferguson	Lilly	Mark Rosolowsky	BMS
Georges France	Novartis	Tom Schultz	J & J
Betsy Fritschel	J & J	Steve Tyler	AbbVie
John Groskoph	Pfizer	Jim Webb	BI
Nirdosh Jagota	Roche-Genentech	Diane Zezza	Novartis
Bob Kelly	Bayer		

PQRI Conference Draws Broad CDER Support

The PQRI conference drew wide attendance from across CDER's CMC and compliance offices, with more than 100 agency personnel participating.

The level of FDA participation was reflective of its need for industry support in ironing out the variety of issues that are now on the table in CDER's effort to create a quality regulatory process that better reflects the advancements in science and technology, risk management, and QbD.

The Product Quality Research Institute (PQRI) was established with FDA backing in the late-1990s to support the regulatory research and development needs of CDER's new Office of Pharmaceutical Science (OPS). The Institute is guided by a steering committee composed of representatives from each of its Member Organizations, which include the FDA, Health Canada, US Pharmacopeia, American Association of Pharmaceutical Scientists (AAPS), Parenteral Drug Association (PDA), International Society of Pharmaceutical Engineers (ISPE), International Pharmaceutical Excipients Council- Americas, and the Consumer Healthcare Products Association (CHPA).

Through its working groups and technical committees, PQRI tackles specific scientific research projects to support the review process in ensuring drug product quality, safety, and performance (*see PQRI.org for an organization chart indicating its current areas of focus*).

Industry's inability to deploy technology advancements and learnings post-approval due to the current CMC review processes across agencies was a dominant theme at the PQRI conference as well as at the PDA/FDA conference held a week earlier.

The dialogue at the two conferences around how to advance the regulatory initiatives underway for breakthrough therapies, drug shortages, quality metrics, global harmonization, generic user fee implementation and quality by design all threw the problems in the current CMC review and post-approval change paradigm into strong relief.

Preceding Nosal to the podium at the PQRI post-approval change session were two FDA OPS officials, Geoffrey Wu and Daniel Peng. They focused on where the agency is now in regulating post-approval changes and how scientific advances are opening up pathways to improve the process. Their presentations reflected OPS familiarity with and openness to the concepts in the PhRMA proposal.

[A full review of Nosal's presentation and the discussions that ensued at the PQRI conference session appeared in the [August/September 2014 IPQ Monthly Update](#). By special arrangement, excerpts of IPQ's extensive coverage of the September PQRI/FDA conference are being made available to the PQRI community. IPQ provides in-depth coverage of emerging drug and biotech CMC and GMP issues and developments with a mission of helping advance and harmonize the quality regulatory process globally. For information on how to take advantage of IPQ's introductory company/organization license fees for 2015, contact Wayne Rhodes (rhodes@IPQPubs.com, (202) 841-9720) or Julia Zimmerman (zimmerman@IPQPubs.com). For more on IPQ, visit our website at <http://www.IPQPubs.com>.]

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IPQ Publications LLC, 7920 Norfolk Avenue Suite 900, Bethesda, MD 20814
Phone: 202-841-5027, Fax: 301-913-0119

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