Cross-industry organizations

An introduction to the Product Quality Research Institute (PQRI)

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What is PQRI?

The Product Quality Research Institute (PQRI) is a non-profit consortium of organizations that work together to generate and share timely, relevant and impactful information that advances global drug product quality, manufacturing and regulation.

Established in 1999 and now marking its 20th anniversary, PQRI originated from a collective effort between the United States Food and Drug Administration (FDA) Office of Pharmaceutical Science (OPS) and several of the industry's major trade associations. Its purpose was to create a safe haven in which scientists from industry, academia and the FDA could collaborate to advance science in support of regulatory guidance.

This idea was embraced early on by senior FDA leadership, including then FDA Commissioner, Jane Henney, MD, who said "PQRI is … an excellent means for leveraging FDA's intellectual and laboratory resources; to promote regulatory research programs designed to enhance the science base that we need to provide, and I am convinced it will be a win, win, win solution for the public, the industry, and the agency."

Over the past two decades, PQRI has coordinated and advanced scientific research and knowledge-sharing that has been leveraged by the FDA and other regulatory agencies to inform decisions on policy and guidance. Through its Technical Committees and Working Groups, PQRI tackles projects to ensure the quality, safety and performance of drug products.

What makes PQRI unique?

- Inclusion of regulatory agencies and standard-setting bodies as members, as well as its distinct organizational structure, which enables direct connections and fosters cross-collaborative pathways between regulators, academia and industry.
- Providing resources to support research projects that serve as stimuli for, and help shape, global regulatory policies.
- Helping member organizations meet their missions by identifying work of broad interest to those organizations' members.
- Providing a platform that encourages and facilitates inter-organizational collaboration and consensus-building.

PQRI goals

1. Promote science-based regulation by developing and delivering a portfolio of projects and public platforms of high value to industry and regulators.

2. Expand membership and outreach internationally to industry and regulatory agencies, to enhance and further diversify expertise and information sharing.

3. Enhance member organization benefits through PQRI activities and work product.

PQRI impact

The impact of PQRI's work on the pharmaceutical product quality field is evident in the breadth of topics PQRI has addressed and the science-based policy decisions PQRI has helped support.

PQRI has published more than 50 research papers and case studies in peer-reviewed scientific journals and organized more than 25 workshops and conferences on a diverse array of topics, including:

- Shelf life stability
- Leachables & extractables [for orally inhaled and nasal drug products (OINDPs) and parenteral and opthalmic drug products (PODPs)]
- Biopharmaceutical classification system
- Manufacturing process robustness
- Manufacturing process drift (detection, measurement and control)
- Container closure
- Biosimiliars
- Elemental impurities
- Process validation
- Blend uniformity

PQRI success stories

Blend uniformity. Industry scientists noted that samples of powder taken from a blended mixture did not show the same degree of active dose uniformity as that of compressed tablets. The FDA initially proposed to test all blends for content uniformity of the active ingredient(s) and reject batches that did not meet established criteria, which would have been expensive and time consuming. In response, PQRI conducted extensive data mining and statistical analyses that confirmed the superiority of testing compressed tablet samples. These findings provided the basis for an enhanced tablet test-

ing scheme, which was adopted by the FDA in 2003.

Leachables and extactables. In 2006, PQRI collaborated with IPAC-RS and submitted recommendations to the FDA on "Safety Thresholds and Best Practices for Leachables and Extractables Testing in Orally Inhaled and Nasal Drug Products." The groups then sponsored a public workshop and a series of training courses based on their work. Three were held in the US, one in Europe and one in Canada (presented to Health Canada). While the threshold approach recommended by this collaborative was not formally put into FDA guidance, it is widely used by industry and regulators in the US and other countries and is now being investigated for opthalmics and parenterals.

Aerodynamic particle size distribution (APSD) profile comparisons. The PQRI's results prompted the FDA to reconsider its approach to bioequivalence testing of inhaled products, specifically APSD comparisons. The chi-square ratio test originally proposed by the FDA for that purpose was sidelined and more appropriate tests were subsequently researched and proposed by the FDA.

PQRI partners throughout the years

PQRI's journey would not have been successful without the dedication and expertise of our many partners, including:

- Association for Accessible Medicines (formerly part of GPhA)
- American Association of Pharmaceutical Scientists (AAPS)
- Biotechnology Innovation Organization (BIO)
- Consumer Healthcare Products Association (CHPA)*
- Health Canada*
- International Pharmaceutical Aerosol Consortium on Regulation & Science (IPAC-RS)
- International Pharmaceutical Excipients Council of the Americas (IPEC-Americas)*
- International Society for Pharmaceutical Engineering (ISPE)
- Parenteral Drug Association (PDA)*
- Pharmaceutical Research and Manufacturers of America (PhRMA)
- US Food and Drug Administration, Center for Drug Evaluation and Research (FDA, CDER)*
- United States Pharmacopeia (USP)*

***Current PQRI Members**

Current PQRI workstreams

PQRI organizes conferences, workshops and webinars that bring together regulators, industry scientists and academics for in-depth discussions on current and emerging regulatory and scientific challenges in pharmaceutical quality.

In April 2019, PQRI held its fourth joint conference with the FDA, a three-day event that provided education for the scientific and regulatory communities on novel approaches to advancing product quality. The conference theme was patient-centricity and more than 75 subject matter experts and regulators from around the world joined PQRI to present new techniques for designing, developing and manufacturing drug products that meet the full spectrum of patient needs.

PQRI also hosts a free quarterly webinar featuring forward-looking biopharmaceutics research studies and regulatory trends. Presenters are subject matter experts from industry and the FDA.

Developing a pulmonary drug product classification system

Another core activity is research and PQRI is currently sponsoring several innovative projects of its own. Over the last year, a team of PQRI scientists from industry, academia and the FDA have been collaborating to develop a pulmonary drug product classification system to aid in and de-risk the development of inhaled drugs. Similar to the Biopharmaceutics Classification System (BCS) developed some 20 years ago, this classification system will be based on biorelevant product attributes. However, the greatest challenge is that the absorption and deposition of inhaled drugs are influenced by many more factors than GI-administered drugs, including regional physiological differences in lung anatomy, fluid mechanics, aerodynamic particle size, device design and patient administration. Additionally, harmonized biorelevant testing and characterization techniques are lacking and the number of pulmonary therapeutics is small compared to oral therapeutics.

Therefore, to establish predictors of bioavailability and efficacy, the team will first use principles-based *in silico* models to simulate local and systemic pharmacokinetic (PK) responses to changes in critical product attributes and validate these tools using available *in vivo* data. Once validated, the team will use these tools to understand how biorelevant product attributes will be expected to influence clinical performance and develop an iBCS classification grid. The team recently gave two presentations on their work at the PQRI FDA joint conference in April and anticipates two more years of collaboration supported by PQRI.

PQRI's future

PQRI welcomes inquiries from trade and professional associations serving the life sciences industry who want to learn more about

the unique role and important mission of PQRI. Organizations and individuals can learn more by contacting the PQRI Secretariat at PQRISecretariat@pqri.org.