Collaborations for Success - PQRI: An Industry, Regulatory and Academic Consortium

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Why Was PQRI Established?

- Dr. Roger Williams, Director of FDA’s Office of Pharmaceutical Science - “Regulation must be based on good science”
  - There is a value in establishing a “safe haven” in which scientists from the pharmaceutical industry and the US Food and Drug Administration can meet to conduct research to support the development of science-based regulatory policy

- PQRI was established to provide this safe haven.
What is PQRI?

- A consortium including FDA’s Center for Drug Evaluation and Research (CDER), Industry, and Academia.
- Established in January of 1996 - guided by a Board and a Technical Steering Committee composed of representatives from its sponsoring organizations.
- PQRI member organizations represent industry, academia, and government and cover a wide array of scientific issues related to pharmaceutical products.
- Through its working groups and technical committees, PQRI tackles projects to ensure the quality, safety and performance of drug products.
Current PQRI Member Organizations

- American Association of Pharmaceutical Scientists (AAPS)
- Consumer Health Products Association (CHPA)
- FDA/CDER
- Health Canada
- International Pharmaceutical Aerosol Consortium on Regulation & Science (IPAC-RS)
- International Pharmaceutical Excipients Council of the Americas (IPEC Americas)
- United States Pharmacopeia (USP)
Original Purpose

"...serve as a forum for academia, industry and FDA to work cooperatively to conduct pharmaceutical product quality research and to support development of public standards..."
Original Mission

To advance science-based pharmaceutical product quality regulation
PQRI Structure

- Board of Directors - administrative management and fiduciary duties

- Steering Committee - responsible for all activities related to scientific operations and scientific decision making

- Technical Committees – Biopharmaceutics, Development and Manufacturing - provide technical and scientific guidance, direction and review for the several Working Groups operating within their technical realm

- Working Groups:
  - Generate, evaluate, and discuss information or data
  - Develop recommendations summarized in technical reports, and scientific papers
  - Coordinate conferences, workshops, seminars and forums to collect input from the larger scientific community and to share the information they have gathered on the specific subject evaluated
First Ten Years

PQRI added great value through a multitude of wide-ranging efforts
Outcomes

- Many success stories
- Focused on science
- Built through a collaborative and inclusive process
- Focused on informing FDA and US regulatory standards and establishing expectations
  - Multiple white papers and recommendations were provided directly to FDA for consideration
  - Output was also shared with the public via workshops and publications
The World Has Changed

- Globalization of the pharmaceutical industry
  - Complex, global supply chains
  - Products marketed globally
  - Regulations both converging (e.g., ICH) and diverging
  - Emerging regulatory authorities

- Existence of multiple organizations that represent pharmaceutical stakeholders with increasingly overlapping interest

- Greater access to major regulatory agencies exists than was available ten years ago – yet fewer FDA Guidances to establish regulatory expectations
What Hasn’t Changed?

- The need for collaboration by industry, regulators around the world and academia
- The need to focus on science
- The need to drive continuous improvement and innovation in a highly regulated environment
- The need for clear product quality standards (ideally global) to establish what good looks like and provide a path to get there
PQRI’s Response to Change

- Determine what, if anything, distinguishes PQRI from other industry associations and focus our efforts in the identified area(s)
- Align mission with the unique contributions PQRI can make
- Ensure that PQRI’s work adds value and drives continuous improvement and innovation in areas of importance to public health
Is PQRI Unique?

- The answer is an unequivocal YES!
  - A survey of the PQRI projects completed and underway demonstrates a singular focus on enhancing scientific understanding to improve product development and quality
  - There are few other opportunities for collaboration in the science of pharmaceutical quality, particularly if laboratory research is a required element
Mission Aligned with Unique Purpose (2009)

“A unique forum to focus critical thinking, conduct research, exchange information, and propose methodology or guidance to pharmaceutical companies, regulators, and standard setting organizations”
Aligned Mission (continued)

“…Working together to generate and share timely, relevant, and impactful information that advances drug product quality and development…”
Meaningful Changes?

- Timely, relevant and impactful
  - Projects must make a difference in the near-term
- Advance drug product quality and development
- Forum for critical thinking, research
  - Focus on science maintained
  - Collaboration maintained
- Guidance to pharmaceutical companies, regulators and standard setting organizations
  - Global focus
  - Inform and influence thinking of all stakeholders for the purpose of continuous improvement and innovation
Our Mission is Important: How Do We Assure Success?

- Skilled and committed volunteers
- Well-defined processes for common PQRI activities
- Culture that rewards innovation in the science of pharmaceutical quality
- Robust scientific projects with meaningful outcomes
- Have outlets that help the outcomes become widely disseminated, established practice
- A steady source of funding driven by the desire to see the right work done and properly disseminated
Volunteers

- PQRI depends completely on its dedicated volunteers
- Volunteers are welcome from all stakeholder communities
  - Those engaged in working groups do not need to belong to a PQRI member organization
Well-Defined Processes

- PQRI must be scientifically driven but run like a business
- Significant enhancements to PQRI processes were implemented in 2009 to ensure that decisions are made and projects move forward as quickly as possible
  - Project identification, development and approval
  - Team formation and volunteer selection
  - Project management, communication, and completion
  - Toolkits and materials are available for volunteer use
Recognition – Rewarding Innovation

- Volunteers do much of their work for PQRI on their own time
- Significant effort is expended during the lifetime of a project
- Whether the project succeeds or fails, PQRI must demonstrate appreciation and recognize the contributions of teams and individuals
  - Excellence in Research Awards
- Volunteers must see that their work has made a difference (widely-used white paper, guideline, report, or standard)
Robust Scientific Projects

- New ideas are always welcomed for projects within the scope of PQRI’s mission
- Proposals can come from any source
- A tool has been developed to allow PQRI to evaluate the value of proposed projects
  - A matrix of questions with scores associated with them
  - End result is a quantitative assessment of the value to public health and PQRI if the project is completed
Value Assessment

● Is it relevant?
  - Regulatory or industry need
  - Are other groups already working on this topic?

● Can it be done in a timely way?
  - Do the resources and expertise exist within PQRI or can they be obtained?
  - What is the time required for completion?
  - What is the total investment required versus the overall benefit?

● Will the project be impactful?
  - How will the end result be used by stakeholders?
  - Will it have the ability to impact current thinking or practices?
Result of Refocused Mission

- Mission was refocused early in 2009 and enhancements were made to work processes
- As before, successful projects continue to be initiated and completed but the pace is accelerating
- Evidence of the impact of the refocused mission is clear with the proposal and approval of several novel and high-impact projects
Biopharmaceutics Technical Committee

Mission - Promote research in the area of biopharmaceutics. Areas of interest include:

- Linkage of in-vitro drug dissolution/release methods to in-vivo drug bioavailability and bioequivalence
- Methods for the determination of bioavailability and bioequivalence, pharmacokinetic-pharmacodynamic relationships and comparative clinical trials

- Current Working Groups:
  - Sequential Design
  - Biopharmaceutical Classification System III
New and Ongoing Projects – Biopharmaceutical Technical Committee

- BCS III
  - Research completed – publication in progress

- Bio 3
  - Contract being drafted for clinical study

- Biosimilars
  - Discussion group exploring potential PQRI projects

- Nanomaterials
  - Contract with Texas A&M to define scope of future work
Development Technical Committee

Mission - Conduct research projects which help to more clearly define through technical examples and applications

- Quality by Design (QbD) concepts
- Science or related activities associated with QbD
- Current Working Groups:
  - Leachables and Extractables
  - Stability Shelf Life
  - Container/Closure
  - Sulfonate Esters
  - QbD
New and Ongoing Projects – Development Technical Committee

- Container Closure Systems
  - Initial research done – possible USP Chapter

- Stability Shelf Life
  - White paper near completion – ready for broader vetting by potential users

- Leachables and Extractables – Parenteral and Ophthalmic Drugs
  - Workshop Feb, 2010. Possible USP Chapter

- PK/BE Workshop report ready for publication
Manufacturing Technical Committee

Mission - Leverage manufacturing expertise to define science-based approaches that

- Appropriately integrate risk assessment
- Encourage innovation and continuous quality improvement in pharmaceutical manufacturing
- Encourage flexibility in the associated regulatory processes

Current Working Groups:
- Specification Design and Life Cycle
- Risk Management Case Studies
New and Ongoing Projects – Manufacturing Technical Committee

- Risk Management
  - Paper ready for publication
- Specifications – Life Cycle and Design
  - Paper approved for publication
- Transdermals
  - Working Group to inform update of SUPAC guidance
- Supply Chain for Excipients
  - Proposal being developed
- Process Drift Workshop – Another Success Story!
Sulfonate Esters: Background

- Concern existed that sulfonate esters may be genotoxic impurities and are potentially formed during drug substance manufacturing when sulfonic acids are used in the presence of alcoholic solvents.
- The elimination of sulfonic acids from drug substance manufacturing would be highly undesirable due to its useful synthetic properties.
- The amount of sulfonate esters formed under synthetically relevant conditions was unclear.
Sulfonate Esters: Objective

- To scientifically demonstrate if sulfonic acids can safely be used in drug substance manufacturing by
  - Understanding the kinetics of formation and decomposition of sulfonate esters during drug substance manufacture under synthetically relevant conditions
  - Determining if conditions can be manipulated to control the levels of sulfonate esters formed
Sulfonate Esters: Impact

● Industry will be able to make use of the analytical method and kinetic information to evaluate specific synthetic conditions to determine the extent of sulfonate ester formation in proposed synthetic routes

● Regulators will have a scientific basis for assessing the appropriateness of synthetic pathways in which sulfonate esters may be formed
Going Forward – Sustainability Via Continuous Improvement

● Are we in the right areas?
  – Biosimilars – can PQRI help develop a standardized comparability (quality) platform?
  – Should we broaden the scope to include other areas such as regulated bioanalysis?

● Should we pursue interactions with Europe (FIP, European regulators and industry organizations) to try to harmonize our output?

● Are there funding sources we’re missing?
  – Grants from regulators or interested parties?
Inputs and Outputs – How Will PQRI Continue to Grow?

- Further tap AAPS Focus Groups for projects with high industry impact
- Continue to focus projects on outcomes that can become standards (USP/ASTM), guidelines or FDA Guidances
- Seek and obtain funding from groups to which the work is of value
- Expand its membership by attracting associations that see value in the outputs
The Future of PQRI

- The future is bright given the unique forum for scientific collaboration that PQRI provides.
- Many opportunities exist to influence thinking across pharmaceutical stakeholders for the benefit of patients.
- Flexibility exists for participation in PQRI, even if the volunteer is not associated with a member organization.
- To remain viable long term, PQRI needs to continue to:
  - Develop and execute meaningful projects
  - Attract the volunteers needed to do the work
  - Have important outputs lead to meaningful standards/guidelines
  - Develop funding mechanisms that assure sustainability
Thank You!