



International Consortium for Innovation and Quality in Pharmaceutical Development



2011 IQ Symposium Report

January 2012

Introduction

Organizing Committee

Chair: Gordon Hansen, Boehringer Ingelheim
Shuhong Zhang, Abbott
Dax Rose, Astellas Pharma US, Inc.
Karen Palermo, AstraZeneca
Winston Brown, Baxter
Mahesh Chaubal, Baxter Healthcare
Pierre Boulas, Biogen Idec
Mary Ringwood, Bristol-Myers Squibb
Kenneth Dammers, Celgene
Patricia Puma, Eisai
Carl McMillian, Eli Lilly
Ingrid Mergelsberg, Merck & Co. Inc.
Wen Chyi Shyu, Millennium
Vic Kadambi, Millennium
Tushar Misra, Sunovion
Jeff Soderquist, Takeda
Daniel Belmont, Vertex, Inc.

The international Consortium for Innovation and Quality in Pharmaceutical Development (IQ), formed in 2010, is a not-for-profit organization of pharmaceutical and biotechnology companies with a mission of advancing science-based and scientifically-driven standards and regulations for pharmaceutical and biotechnology products worldwide.

The IQ Consortium held its first annual symposium, "The Pursuit of Innovation in Pharmaceutical Development" on November 30, 2011. The Symposium was attended by almost 200 participants from 28 IQ member companies and other industry associations, and featured an exceptional faculty of speakers, moderators and panelists from within and outside of the pharmaceutical industry. Through a combination of podium presentations, panel discussions and poster sessions, participants reviewed and discussed examples of innovation efforts made by IQ member companies and IQ Working Groups, challenges which IQ is uniquely positioned to address, and how experiences and lessons from other industries can illuminate these efforts.

The IQ 2011 Symposium inspired much creative thinking among participants, judging by feedback from the Board of Directors and other Consortium members, making participants eager to implement the concepts they learned at the Symposium to foster innovation in their departments, organizations and lives.

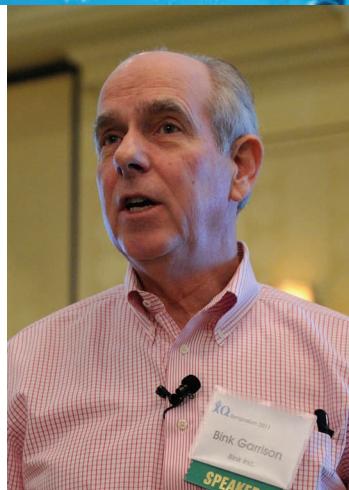
The Symposium program and slide presentations are available [here](#).



The Emergence of the IQ Consortium: Origins and Aspirations

Terry Tougas, Chair, IQ Consortium, Highly Distinguished Research Fellow, Boehringer Ingelheim

Dr. Tougas presented the formation history, mission, objectives and activities of the IQ Consortium. In the short time since its formation in late 2010, IQ has marshaled the industry's scientific resources, established a strong organizational framework, set clear priorities and broadly engaged regulatory communities and other stakeholders. IQ serves as an incubator for innovative and multi-disciplinary scientific collaborations and is rapidly becoming a leading voice for innovation and quality in pharmaceutical development.



Innovation is Not about Science

Bink Garrison, Founder, Bink Inc.

Corporate Life Cycle Disease (CLCD) is, according to Mr. Bink Garrison, a disease to which many companies succumb as they advance through their early years into maturity. It is characterized by changes in culture and ways of thinking that focus less on innovation and experimentation and orient the company's thinking instead toward finding "the most efficient way to grow and deliver value to shareholders (this quarter)." This in turn leads to "rational decisions that strive to reduce uncertainty and lower risk" and results initially in "predictable earnings generated by optimizing existing markets and technologies," but ends in mortality.

Building flexibility into corporations, however, simultaneously fosters effective functioning and encourages activities that will perpetuate the wellbeing of an organization, thus curing (or preventing) CLCD. This can be accomplished through the creation of a positive culture by individuals at every level of the organization who recognize that while certain decisions and changes may generate discomfort or unpopularity in the short term, they will produce significant benefits in the long term.

To illustrate how innovation can be fostered, Mr. Garrison led the symposium attendees in four exercises:

1. Fractal Innovation Scrum One: Conditions for Innovation
2. Fractal Innovation Scrum Two: Organic Innovation Leadership
3. Deviant Conversation
4. Predictive Conversation



These required attendees to interact extensively with each other and generated conclusions about the top ten conditions needed for innovation and the top eight ways to lead organically.

Top Ten Conditions Needed for Innovation:

- | | |
|-----------------------------------------------|-----------------------------------------|
| 1. Clear, agreed vision, objective & timeline | 6. Urgency/sink or swim/nothing to lose |
| 2. Empowered teams | 7. Dedication, passion |
| 3. Pressure: time, money, fear of failure | 8. Hard but achievable goal |
| 4. Diverse teams | 9. Trust within the group |
| 5. Open, intense discussion | 10. Important problem |

Top Eight Ways to Lead Organically:

- | | |
|-----------------------------------------------------------------------------------|-----------------------------------------------|
| 1. Remove toxins; purify; filter | 5. Re-energize the whole system |
| 2. Work collaboratively with other systems; communicates; enables other functions | 6. Handle complex inputs and situations |
| 3. Work autonomously when needed | 7. Break down problems into manageable pieces |
| 4. Respond to needs and stresses | 8. Support, strengthen the whole body |



In conclusion, Mr. Garrison encouraged participants to build cultures that make innovation possible, collaborate, seek out and use tools from other industries, and take responsibility for inciting innovation.

Green Chemistry Innovations

Richard Williams, American Chemical Society Green Chemical Institute



Dr. Richard Williams' talk explored green chemistry as an approach for achieving sustainable performance and economic advantage, "driven by innovation, enabled by collaboration, and catalyzed by a vision of the future, science and technology, and a commitment to pursue and apply knowledge." He discussed the scope of green chemistry and the advantages it provides, the ability it has to meet challenges, opportunities for IQ companies, and how to inspire innovation in green chemistry. Both a roadmap for green chemistry and a roadmap for green engineering were presented in his talk, followed by an assessment of the significant problems that will face humanity in the next several decades, including energy, water, food, and environment.

For the pharmaceutical industry specifically, Dr. Williams highlighted manufacturing, design of biologics, design for bioavailability/targeting, and design for degradation/lower toxicity as priority opportunities for more thorough application of green chemistry concepts; he also highlighted a program at an individual company as well as the American Chemical Society Green Chemistry Institute as means of advancing the science around and implementation of green chemistry.

Innovation Happens at the Vertices: How Collaboration Across Traditional Boundaries Drives Excellence and Innovation in Pharmaceutical Development

Patricia Hurter, PhD, Senior Vice President, Global Pharmaceutical Development, Vertex

Dr. Hurter's presentation focused on case studies from her own company, related to drug product development and manufacturing, as well as continuous processing, demonstrating how innovation is fostered when people of diverse experiences and knowledge are able to work together on specific projects -- "innovation happens at the vertices."

Dr. Hurter discussed how working with others spurred innovation in development of the product Incivek (telaprevir); progress on biopharmaceutical modeling and the company's plans to implement continuous processing. Regarding development of Incivek, she noted how collaboration with others both outside the company and within helped to





address a variety of very complex challenges, with innovations developed such as new ways to use existing techniques to measure phase transitions of the API (amorphous to crystalline) suspensions. People from manufacturing, process chemistry, analytical, materials, and suppliers collaborated to better understand and overcome serious challenges with drug product stability. Similar collaborations with experts within as well as outside the company were accomplished to make significant and successful advances in spray drying technology for the product. The company continued collaborative opportunities with regulators, quality and technical operations to drive a QbD-based application.

For biopharmaceutical modeling, Dr. Hurter emphasized that in order for advances in this area to be truly successful, effective collaboration must be established among CMC, safety, clinical, materials and formulation entities in and out of the company. Modeling holds a great deal of promise for improved drug products with decreased use of animal studies, and can be used as a tool to integrate input from a number of diverse departments.



Dr. Hurter closed her talk with thoughts on continuous processing, which could significantly improve quality with the capability of real-time release and continuous monitoring, and represents a significant step toward QbD. Implementation could potentially help companies save, or use more efficiently, large amounts of resources.

Collaboration and Innovation in Early Stage Development

Steven King, PhD, Divisional Vice President GPRD, Development Sciences, Abbott



Dr. Steven King started his talk by summarizing the challenges facing the pharmaceutical industry, including the increased research and development costs, the declined success rates of target identification, enhanced competition among companies, as well as tightened scrutiny by regulatory agencies and other stakeholders.

Dr. King then drilled deeply into identifying solutions to these challenges and advocated that “pre-competitive collaboration across the industry is a “Must Have” for future industry success”. Focusing on the late discovery and early development phase, which was highlighted as a particular dynamic and crucial time period for drug development, Dr. King shared with the audience innovation experiences in Abbott in a variety of functional areas, including toxicology studies, candidate optimization, statistics, CMC (Chemistry, Manufacturing and Control), implementation of the 3Rs (Replacement, Refinement and Reduction) concept and infor-

“IQ is here to share ideas, share refinements, share implementations, successes and challenges.”

audience innovation experiences in Abbott in a variety of functional areas, including toxicology studies, candidate optimization, statistics, CMC (Chemistry, Manufacturing and Control), implementation of the 3Rs (Replacement, Refinement and Reduction) concept and infor-



mation management. Using these examples, Dr. King demonstrated that collaborations within and across scientific disciplines have greatly facilitated innovation and led to success.

Dr. King ended his talk by encouraging IQ companies to collaborate in the pre-competitive space on as many topics as possible, and emphasizing that "IQ and efforts like it will be critical for future success."

Innovation in Biologics Manufacturing

Jorg Thommes, PhD, Vice President, Global Engineering, Biogen IDEC



Innovation in manufacturing execution (as distinct from innovation in manufacturing process) could serve as an important source of added value in today's business environment. Statistical design of experiments (DoE) is already being used to identify key parameters for manufacturing control and to establish their design space. An innovative approach to DoE takes it a step further by breaking up the process into smaller modules and integrating feedback loops in the process models and controls. Such 'partition design' can bring about a better understanding and control of the process with potentially fewer experiments.

Another presented example of innovation-in-execution was a case study of a centrifuge scale-down. The scaled-down model was composed of two steps/pieces of equipment, each representing a critical contribution to centrifugation: a capillary shear device and a lab-scale centrifuge.

Finally, a critical examination of the extensive amounts of available data may uncover possible control tools that may enable a smarter manufacturing execution. For example, the scores of variables describing an AIEC chromatogram could be assessed for their importance and ability to predict some quality attribute of the drug substance. Controlling the few parameters with quantitative correlation to a drug substance attribute enabled an improvement in process robustness. In addition, innovative manufacturing infrastructure, such as use of single-use equipment, can help increase efficiency of manufacturing execution through added flexibility in time and location for setting up manufacturing sites.

Summaries of Panel Discussions

- ★ Innovation is doing things better today than we were doing them yesterday. Innovation has four phases: clarification of the problem, ideation of solution, design of solution and implementation.
- ★ For a company to achieve innovation across the whole spectrum of the business,





from discovery to marketing and to lifecycle management, innovation has to be elevated as a cultural initiative.

- ❖ Building an innovative culture which stimulates open discussions and interactions among employees is a good way to facilitate the implementation of innovative concepts at companies.
- ❖ Engaging the regulatory agencies at all levels proactively, upfront and persistently is essential to obtain agencies' support for innovative ideas and approaches, such as modeling and QbD. IQ is well positioned to undertake these communication and education initiatives.
- ❖ Statistics is becoming increasingly important in the industry. Potential approaches to training employees to understand statistics concepts were proposed and discussed.
- ❖ Enhanced collaborations between experts in biomarker identification/validation and clinical pharmacology can potentially address challenges faced by clinical trials with personalized medicines.
- ❖ In the course of innovation, it is important to ensure that quality is not compromised. This can be done through enhanced quality control conducted by a cross-disciplinary team of experts.



***“With 90% attrition rate [in this industry]...
precompetitive collaboration is a must.
Otherwise, it will be not the last company standing wins,
but the last one standing gets to put out the light.”***

