



Innovative Approaches to Quality: 2012 IQ Symposium Report

SYMPOSIUM ORGANIZING COMMITTEE

- ◇ **Chair: Pierre Boulas, Biogen Idec**
- ◇ Shuhong Zhang, Abbvie
- ◇ Mark Gold, Boehringer Ingelheim
- ◇ Gordon Hansen, Boehringer Ingelheim
- ◇ Dennis O'Connor, Boehringer Ingelheim
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The second annual IQ Consortium symposium, “Innovative Approaches to Quality”, was held December 5, 2012. Attended by approximately 200 participants, it featured an exceptional faculty of speakers and moderators from within and outside of the pharmaceutical industry.

Keynote Address: Quality and Regulation

Janet Woodcock, Director of Center for Drug Evaluation and Research (CDER), FDA

Quality is the basis of all pharmaceutical development processes. Historically, FDA implemented quality regulations in response to “bad actors” in the industry who proceeded with minimal effort. However, FDA recognized this increased the regulatory burden in manufacturing, while limiting innovation. To mitigate this, FDA implemented its Pharmaceutical Quality in the 21st Century program in 2002.

Quality by Design (QbD) and Manufacturing Innovation

Early adapters are already benefiting from QbD, which has significantly improved the transfer from development to commercial, led to fewer late surprises in commercial production, less Corrective Actions/Preventative Actions (CAPAs), and less waste due to better process and product understanding.



Regulatory review has not yet changed greatly, and inspections are variable. There is variability in industry commitments to QbD implementation. Further, the economic downturn reduced enthusiasm for QbD investment. FDA recognized the importance of reevaluating its efforts, and the user fee program is encouraging this reevaluation. Manufacturing and scale-up may be the rate limiting step in bringing innovative drugs to market in the future. Delays in approvals often occur because a company’s commercial scale manu-

facturing needs improvement.

Dr. Woodcock raised the question of whether the pharmaceutical industry considers quality to be a competitive advantage. She noted that innovators that have access to quality will be better able to transfer to a commercial scale. Targeted products are very expensive due to R&D, but there could be a business case for innovators to move to technology such as robotics, continuous manufacturing, or statistical process control.

Breakthrough Drugs

New targeted therapies are highly effective. Breakthrough drugs have been a ‘game changer’ for many therapies, and Congress has passed legislation supporting a regulatory process for addressing breakthrough drugs. Based on clinical data, FDA can designate a drug as a breakthrough drug and work with the innovator to identify the most parsimonious drug development program for eventual approval. When a drug is very effective, companies ideally should be able to facilitate clinical trials and availability of clinical trial samples for further study.

Manufacturing and Supply Chain Quality and Security

Many health care providers remain unaware of the risks involved in buying drugs from the internet. There is some understanding that drug shortages relate to the ability to manufacture high quality products. Risks related to globalization, counterfeit, and shortages are also related to quality.

Regulation and FDA Structure

Dr. Woodcock questioned the sustainability of the current method of regulating, given globalization. The generic drug program has led to proliferation of establishments worldwide, while pro-

duction of new molecular entities has decreased.

The regulatory system is prescriptive, and Dr. Woodcock asked if the system could be improved with an equal or higher product approval rate. The FDA is therefore reorganizing its quality function by developing a pharmaceutical quality department and combining compliance and review. FDA is also establishing a surveillance



function to look at data and metrics. Their goal is to have a more uniform approach to quality, and formal establishment is expected within 6 months. FDA will also aim for equal expectations for facilities around the world. FDA/CDER is moving to an ‘expertise’ structure, where review of a new drug is done by specialist groups. FDA is continuing its program to work on QbD, but industry has to opt into QbD. There is also a need for better application of statistical approaches to sampling and a better scientific basis for standards. Attention to drugs that the public is consuming in high volume is needed. All drugs, including those produced by compounding pharmacies, should be held to the same quality standard.

In conclusion, Dr. Woodcock called for all parties to work together to bring the drug manufacturing enterprise to a higher level and to jointly propose a path forward.

Productive Conversations in Science-Based Organizations

Matt Kayhoe, Kayhoe Consulting



Mr. Kayhoe discussed how to increase the productivity of conversations.

Mr. Kayhoe gave an interactive presentation on improving workplace conversations. Productive conversation is equivalent in complexity to science, and the two are interdependent. Documents are not driving forces within an organization; rather, conversations about documents drive activities.

Mr. Kayhoe discussed a scale of conversations. A conversation where one party is “tuned-out” is the low end of the scale, while the generative conversation where both parties are actively engaged and collaborating is at the upper end.

To increase the productivity of a conversation, one needs to be self-aware of where one is on the scale, be awake and engaged in the conversation, recognize one’s own needs, and acknowledge the need to fuel a relationship. If a relationship is deemed important, one should make an effort to regularly push conversations with this person higher up on the scale.

When conversations are unproductive, it is easy to label the other party as ‘unreachable’. This relieves one of responsibility, but Mr. Kayhoe emphasized the im-

portance of working collaboratively and taking ownership of the problem to move the conversation forward. It is important to always move towards the other person, and to voice any issues. It is also vital to understand the frame of reference that each person brings to a conversation.

Organizations are often based on a chain of command, but function in an inter-networked fashion. Mr. Kayhoe emphasized the need for an organization’s culture to allow for internet-working. (<http://www.kayhoe.com/>)



Dr. Austin speaks with attendees.

NCATS: Catalyzing Transitional Innovation

Christopher Austin, Director, National Center for Advancing Translational Sciences (NCATS), National Institutes of Health (NIH)

Established at the end of 2011, the National Center for Advancing Translational Sciences (NCATS) is a unique NIH center with a mission to “catalyze the generation of innovative methods and technologies that will enhance the development, testing, and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions.”

Dr. Austin presented a number of initiatives NCATS is currently undertaking, such as the NIH Chemi-

cal Genomics Center, RNA Interference, Toxicology in the 21st Century, Microphysiological Platforms, Therapeutics for Rare and Neglected Diseases, and Bridging Interventional Development Gaps programs under its Division of Preclinical Innovation. Its division of Clinical Innovation sponsors Clinical and Translational Science Awards, as well as the Small Business Innovation Research and Small Business Technology Transfer program. Dr. Austin also introduced a new NCATS pro-

gram to identify new therapeutic uses of compounds deprioritized by pharmaceutical companies.

Finally, Dr. Austin summarized NCATS’ main functions as a catalyst for translational innovation and as a hub for collaboration within and beyond the NIH. He called for broader collaborations among governmental agencies, the private sectors and other stakeholders, and expressed strong interest in collaboration with the IQ Consortium. (<http://ncats.nih.gov>)



Dr. Austin and Dr. Tougas.

Innovation— A New Identity for Quality

Juan Torres, Senior Vice President, Global Quality Assurance, Biogen Idec

Innovation, according to Dr. Torres, “should not be an end on to itself but should have a focused objective directed to bring a tangible benefit that can be recognized and quantitated” and “offers a great opportunity for quality professionals to lead by driving improvement in the quality of business, including profitability.”

In today’s Quality organizations, the ability to innovate is vital to sustained success due to the increasing complexity of scientific problems, regulatory requirements and risk management issues. However, building and reinforcing capacity to innovate is not a simple task. By sharing a number of examples and case studies on how innovation skills can be taught and

spread across an organization, and how successful innovation can improve quality, regulatory compliance and efficiencies, Dr. Torres encouraged the audience to be proactive and open-minded, embrace diversity, forgive mistakes and support experimentation. Dr. Torres ended his talk by emphasizing that “innovation can and should become an identifier for Quality organizations.”



Winning the Fight of My Life

Greg Cantwell, Stage IV Glioblastoma Survivor and Caregiver

Mr. Greg Cantwell, a Stage IV Glioblastoma survivor, provided a patient perspective on innovative approaches to quality in medicine. Mr. Cantwell, who was given 5% likelihood of living one year after his diagnosis in 2004, remains cancer-free today after surgery and aggressive chemotherapy. He now provides support to cancer patients and caregivers worldwide through his own non-profit organization.

Mr. Cantwell's program focuses on seven items: 1) statistics versus individual patients; 2) effective communication; 3) personal relationships; 4) positive attitudes; 5) eating well; 6)

strategies that he found effective and ineffective; and 7) transitioning from a survivor to a caregiver.

In particular, Mr. Cantwell emphasized the importance to him of having an active role in his own treatment. He noted that having the right information at hand was crucial in enabling him to take ownership of his treatment, citing how oral and intravenous chemotherapy can be of equal cost in some states, while different in others. Mr. Cantwell underscored the importance of communication and flow of information between pharmaceutical companies, health care practitioners, and patients.

(<http://www.gregsmmission.org>)



A Poster Reception held the night before the Symposium featured posters for many Working Groups.



Public-Private Partnership Approach to Drug Development and Disease Elimination for Infectious Diseases in the Developing World

Charles Knirsch, Vice President, Clinical Research Head, Specialty Therapeutics, Pfizer Inc.

In the past, civil society did not believe product donations were sustainable for purposes of disease elimination yet through several private sector partnerships over the last two decades, industry is now recognized in the World Health Report on Neglected Tropical Diseases as a critical partner in the success of Public Private Partnerships for drug development and Neglected Tropical Diseases elimination.

One example is the scientific and organizational effort towards The Global Elimination of Trachoma by 2020 (GET2020). Trachoma is the most common cause of infectious blindness worldwide and is caused by an ocular chlamydia strain. Children are infected repeatedly and their caregivers, predominantly women, disproportionately

are at risk for blindness in these less developed countries. The International Trachoma Initiative's [www.trachoma.org] basic approach to disease elimination combines knowledge of trachoma control gained over the past 50 years as well as more recent studies of risk factors for disease, blindness, and the WHO-recommended **SAFE** strategy, which includes 1) **S**, the simplified lid surgery for the in-turned eyelashes that will halt pain and corneal damage; 2) **A**, antibiotics for active infection using single-dose oral Zithromax; 3) **F**, clean faces especially in children through sustained behavior change; 4) **E**, environmental improvement to increase access to water and sanitation. Program integration of other disease elimination programs have been facilitated by performing drug interaction studies and also by performing analyses utilizing ad-

vanced modeling techniques. A compartmental model to explore azithromycin and ivermectin PK data was developed and 1000 interaction studies were simulated *in silico* to explore high ranges of ivermectin values that might occur and in effect setting tolerance levels that reassured program activities to combine the therapies to utilize scarce country resources available for mass drug administration. The analyses led to further study of co-administration of azithromycin with the widely used agents ivermectin and albendazole, under field conditions in disease control programs that also did not show serious adverse events in a large study in Mali. Currently, The International Trachoma Initiative is scaling up to 70 million doses annually and the goal to eliminate blinding trachoma by 2020 is within reach.



Allotrope Foundation

James Roberts, Senior Scientific Investigator, Lab Automation Platforms, GlaxoSmithKline

The Allotrope Foundation is a new consortium formed in 2012 as an outcome of an effort started within the IQ Consortium's Analytical Leadership Group Laboratory Information Standards Working Group. The goal of the Allotrope Foundation is to develop a common framework for analytical laboratory data and information management. The Foundation will implement open document standards, an open metadata repository and open source class libraries, using existing standards and tools as appropriate.

The Foundation has met with instrument and software vendors, who expressed support for this pharma industry-led initiative.

The Allotrope Foundation's efforts will provide significant industry-wide innovative technical benefits, for example by reducing data exchange costs and data management costs; by reducing errors in data records; and by enabling automatic generation of regulatory submissions, reports and internal documents. Companies participating in the Allotrope Foundation directly will additionally benefit

from an opportunity to shape solutions, from an early understanding of the developed solutions, and from possible member-only deliverables, such as data converters.

Allotrope's founding members are Abbott, Amgen, Baxter, Boehringer Ingelheim, Bristol-Myers Squibb, Eisai, EMD Serono, GlaxoSmithKline, Merck, Pfizer and Vertex. Any interested pharmaceutical or biotechnology company may join Allotrope Foundation. (<http://www.allotrope.org>)



Panel Discussion

Moderator: Pierre Boulas, Director Analytical Development, Biogen Idec; Chair, IQ Symposium Organizing Committee



Jon Clark, Charles Knirsch, James Roberts, and Pierre Boulas participated in the panel.

Participants

- ◇ **Greg Cantwell**, Stage IV Glioblastoma Survivor and Caregiver
- ◇ **Jon Clark**, Associate Director for Regulatory Policy, Office of Pharmaceutical Science (OPS), Food and Drug Administration (FDA)
- ◇ **Matt Kayhoe**, Kayhoe Consulting
- ◇ **Chuck Knirsch**, VP, Clinical Research Head, Specialty Therapeutics, Pfizer Inc.
- ◇ **Juan Torres**, Senior VP, Global Quality Assurance, Biogen Idec
- ◇ **James Roberts**, Senior Scientific Investigator, Lab Automation Platforms, GlaxoSmithKline



- ◇ Mr. Kayhoe emphasized the need for conversation as a means for communications. He pointed out that scientists often rely on their documents, which will not replace the influencing value of conversation. Trust and cooperation are built through interaction, particularly listening and non verbal signals.
- ◇ Mr. Clark noted the FDA was focusing on improving consistency among FDA reviewers, especially on CMC issues. The FDA created specialized groups to focus on this effort, in order to advance this group while not interfering with other activities.
- ◇ Mr. Clark also noted more information on CMC review of GMP issues will likely be available during the first half of 2013.
- ◇ Dr. Torres indicated why it was imperative to look at how we measure quality in new and innovative ways. Ultimately, resources should be applied in the best way. To make parametric release practical and usable, it is necessary to look at risks and science, not at expectations instituted before.
- ◇ Dr. Torres noted that it is necessary to consider what is required for high quality in order to eliminate boundaries. There is an opportunity to re-evaluate what is being done, and how it could be done more efficiently.
- ◇ When asked how to improve communication with the public and patients, Mr. Cantwell said it would be very beneficial to be able to provide a package of materials to patients and physicians.



Juan Torres, Greg Cantwell, and Matt Kayhoe were also panelists.

- ◇ Dr. Knirsch noted that a path existed for accelerated drug approval for rare diseases. However, manufacturers have to deal with the supply chain and limited distribution. Science is moving very fast, and open source concepts, transformative clinical trials and reanalysis of data should contribute to breakthroughs within the next five years.
- ◇ When asked how Allotrope differed from earlier groups that had tried to create data standards, Dr. Roberts noted that this was the first time the effort had been led by the pharmaceutical industry. Initial focus will be on CMC and discovery, although the concepts will eventually be applied more broadly. Allotrope will have its first deliverables within three years, and will begin software coding in 2013.

“Innovation is not doing the same thing over and over again. It’s about getting to slightly better decisions at every step.”

-Dr. Lew Kinter

IQ Consortium Recognition Awards Presentation

The following individuals were recognized for their contributions to the IQ Consortium:

- ◇ **Mike Sinz** – Leading development of IQ comments on FDA’s Drug-Drug Interaction Guidance
- ◇ **John Orr** and **Shuhong Zhang** – Leading development of IQ comments on FDA’s “Regulatory Classification of Pharmaceutical Co-Crystals” guidance
- ◇ **Brent Kleintop, Tony Mazzeo, Jamie McElvain, Andy Rignall, and John Skoug** - Leading development of five articles on “GMPs in Early Development” in *PharmTech*
- ◇ **Gordon Hansen** - Chair of 2011 IQ Symposium Organizing Committee
- ◇ **Pierre Boulas** - Chair of 2012 IQ Symposium Organizing Committee
- ◇ **James Roberts** - Spearheaded the establishment of “Allotrope Foundation”



Reducing Our Footprint IQ reduced the impact of this conference on the environment by limiting print materials, minimizing the use of disposable products and bottled water, incorporating local and organic ingredients into menus, and encouraging participants to use more environmentally friendly transportation options, including mass transit.



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<http://iqconsortium.org/>