INTERNATIONAL CONSORTIUM for INNOVATION & QUALITY in PHARMACEUTICAL DEVELOPMENT

2015 IQ Symposium Report

Past. Present. Future.

The fifth annual IQ Consortium Symposium, "Past, Present, and Future," was held at the Westfields Marriott in Chantilly, Virginia, on October 21st, 2015. The Symposium was a celebration of IQ's accomplishments during its first five years, and focused on the future and how IQ can continue to drive science and innovation and to benefit patients. Over the course of the day, participants had the opportunity to learn from speakers, discuss issues with other attendees facing the same challenges as themselves, and offer input to IQ leadership about the direction they would like to see IQ take over the next five years and beyond.

FDA Perspective

Lawrence Yu, Deputy Director of Office of Pharmaceutical Quality, US Food & Drug Administration

In 2002, FDA unveiled its "cGMP for the 21st Century" initiative, with the final report appearing in 2004. Since then, significant progress has been made. In the 10 months of 2015, ten guidances for industry have been released. At the same time, industry and FDA have faced growing challenges, such as product recalls and drug shortages, increased globalization of the supply chain, as well as aging manufacturing facilities. FDA's re-organization earlier this year is helping meet the challenges, e.g., through an integrated approach and team-based reviews and inspections. This allows the agency to have "One Quality Voice". The Office of Pharmaceutical Quality's "One Voice Statements" are aiming to impact culture and emphasize patient's involvement. The IQ consortium could help by providing scientific input on the draft guidances and other open issues. Currently, FDA is particularly interested in industry's feedback on dissolution methods for BCS Class I and III immediate release dosage forms, impurities (metals, residual solvents, etc.), BCS biowaivers (which soon will be discussed with Japan's PMDA), BCS class II and IV for modified release, quality metrics, established conditions, analytical methods and procedures, size/shape and other attributes, near IR, environmental assessment, allowable excess volume and vial fill size, as well as botanicals. Larger overarching issues awaiting new or improved approaches are clinically relevant specifications, process capability, continuous manufacturing, 3-D printing, breakthrough therapies, statistical approaches to quality, and biosimilars.

In response to questions from the audience at the IQ Symposium, Dr. Yu clarified that the Agency plans to conduct 5 pilot-program inspections by the end of this year, and there are a total of 20 inspections in the pilot; depending on the outcome of this first phase, the Agency would decide whether and how to proceed with phase 2 of the pilot. He also clarified that the re-organization at CDER is not mirrored by CDRH but the drug center is consulting with the device center on products that involve both drug and device.

Clinical Trials

Craig Lipset, Head of Clinical Innovation at Pfizer R&D

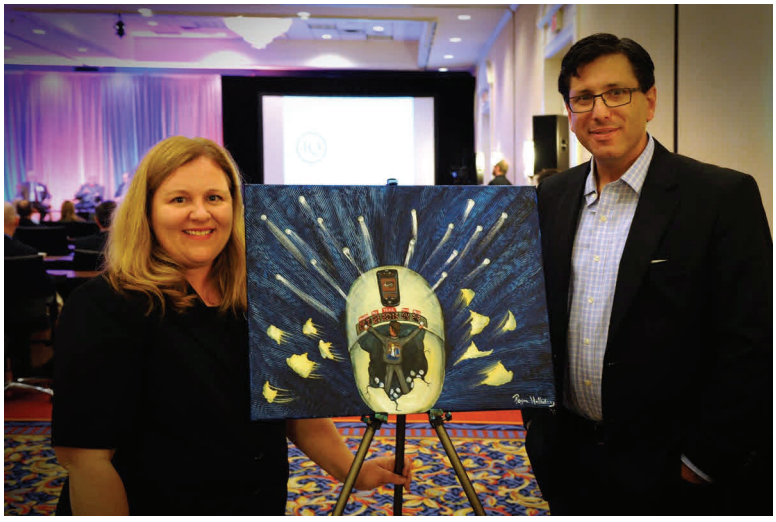
The talk given by Craig Lipset, Head of Clinical Innovation at Pfizer R&D, "Innovation in Clinical Trials: Trends & Potential Futures," shifted the focus of the morning from regulatory perspectives and development to patient engagement in clinical trials, and how technology is changing the way that patients and drug companies are approaching clinical trials. He began by talking about Jeri Burtchell, a woman who enrolled in the Gilenya trial and began blogging about her experience after her screening visit, with whom Mr. Lipset was able to connect after reaching out on Twitter. Mr. Lipset then discussed greater use of technology in clinical trials by drug companies, and how platforms that are changing the way data is collected and shared, such as Patients like Me, with implications for patients as well as the pharmaceutical industry. Technology is likely to continue to be used for data collection, sharing and use, particularly as devices proliferate and tools such as the Apple Research Kit become more widely available, and changes in the healthcare system will create opportunities for decreasing costs and improving outcomes. At the conclusion of his talk, Mr. Lipset described the future as "engaged patients actively participating, empowered by mobile tools, with data captured from electronic sources, conducted within healthcare settings, evaluating multiple medicines with shared infrastructure."

Patient Advocacy

Regina Holliday, Patient Rights Activist, Artist, Author and Founder of the Walking Gallery

Ms. Holliday provided crucial patient perspective on the need to empower patients through access to their medical records and active engagement with health care professionals. Ms. Holliday's husband passed away from Stage IV kidney cancer after several misdiagnoses and a serial lack of communication between health care providers and Ms. Holliday's family. Ms. Holliday was unable to help her husband receive better access to medical care using all of the tools at her disposal. She now works to ensure that other patients and their families are able to access medical information, communicate with health care providers, and obtain the information needed to make educated treatment and end-of-life decisions. Since 2009, Ms. Holliday has concentrated her advocacy work in attendance at public FDA meetings, healthcare-focused conferences, and paintings of medical information to raise awareness of the need to better educate patients.

According to studies, access to medical records and doctor notes results in greater patient adherence to treatments. Ms. Holliday believes patients should have the ability to direct where their records are stored and to view accurate, up-to-date information on their conditions. Tools allowing patients in clinical trials to communicate with one another also promote knowledge sharing to enhance information available to doctors and to their patients.



Disruptive Technologies
Dan Fletcher - Professor and Chair of Bioengineering, UC Berkeley and Founder of CellScope

The history of microscope invention goes back centuries. The first microscopes, however, were not only limited in technical capabilities but were also available only to those who could afford scientific pursuits at a time when science was a hobby of the privileged few. One of the new technologies disrupting status quo in the 21st century makes microscopy accessible to anyone with a cellphone camera, and powerful enough to make the invisible disease agents visible, in a matter of minutes.

A system built by Dr. Fletcher and his students utilizes a magnifying lens set up, a cellphone camera, and software data processing to identify blood parasites from just a few blood droplets taken from patients in the field. The system is imaging in the bright-field mode but can also work with fluorescence and even transmission fluorescence. With contrasts, the resolution can be increased further. The system produces useful data while being compact, robust, and simple to use.

Successful field testing has been conducted with mircofilarial vectors such as Loa Loa, which is similar to that causing river blindness, a devastating disease affecting millions of people, mainly in Africa. A mass drug administration program had been put in place to combat the disease. It had to be stopped, however, when it was found that patients co-infected with Loa Loa experience severe adverse effects when given the drug. Identifying vulnerable patients before administering the drug is therefore critical to the ongoing public health efforts in the affected countries. The current methods for quantifying microfilarial load take three days to return the results. Using the mobile technology developed I n Dr. Fletcher's lab, the analysis takes about 5 minutes. The custom-made software app installed in cellphones control all aspects of imaging and data analysis, including exposure, focus, illumination, data collection, signal/noise detection. About fifteen thousand patients have been treated with the use of technology so far. The group is now developing a range of devices that will enable to move the data collection of our large hospitals to small health-care kiosks. Besides blood infections, devices might be employed to detect TB, malaria, ear infections, as well as be used for environmental testing, such as water quality and coral reef monitoring.

In response to questions, Dr. Fletcher recognized that validating the new device would require some work, but he pointed out that FDA had already approved cellphone based devices (e.g., an otoscope integrated with a cellphone) as a Class I device. He also explained how their new device could ensure specificity, i.e., identify only target parasites and filter out other disturbances that might influence the motion of blood cells.

EDQM Perspective

Cathie Vielle - Head of Department, European Directorate of the Quality of Medicines, European Pharmacopoeia

The Council of Europe includes 47 member states with a total population of 800 million people. By contrast, European Union has 28 countries with a population of 500 million people. EDQM is a Council of Europe's directorate (not to be confused with the European Council). EU Commission approves (not writes) guidances. EMA does not function in the same way as US FDA; but rather EMA is coordinates and supervises national authorities. EDQM oversees the European pharmacopeia (PhEur), both the official standards and the official medicines control laboratories. PhEur is mandatory in 34 member states and in the European Union. It has 28 observers, of which 26 are individual countries plus TFDA and WHO. The PhEUr Commission is a decision making body. All decisions are taken by consensus, which may translate into long timelines if even one member disagrees. There are 70 groups working on PhEur, covering a range of topics from chemicals to herbals and biologics standards. About 700 experts work in PhEur groups, with representatives from industry, regulatory bodies, hospitals and universities.

Observers (such as FDA and TGA representatives) participate not for harmonization purposes but for identifying ways forward. The harmonization occurs through the Pharmacopeial Discussion Group (PDG), which includes USP, Japanese Pharmaceopeia and PhEur Commission, and applies to product monographs, and, retroactively, to excipients. There are two main processes for monographs – "Elaboration by manufacturers" (multisource) and "Single Source Product" (elaborated by regulators only but applicable to all future products).

Besides the PhEur, there are National monographs in some countries (because a topic is of interest only to that country). Several countries have discontinued national pharmacopeias (e.g., Sweden, Finland, Netherlands, etc.), while UK and Spain maintain theirs, which incorporate PhEur. Third-country pharmacopeias (e.g., USP) might be acceptable in Europe but analytical procedures must be validated. The process of monograph creation is transparent, with drafts and style guides available online, and public hearings arranged as needed.

EDQM welcomes input from the industry and particularly the IQ Consortium. There are several ways in which IQ could get involved, including meetings (web, phone, in person), on such topics as new texts and new fields for PhEur; participation in workshops and hearings organized by EDQM; and nominating experts to the PhEur committees once public nominations get allowed – a rule change is under way and will be announced when it is in fact adopted.

IQ at Year 5: Reflections and Visions

Dr. Steve King, Dr. Terry Tougas, and Dr. Lew Kinter, the Chair of the IQ Consortium and the two previous Consortium Chairs respectively, responded to questions from both the moderator, Dr. Dennis O'Connor, and the audience regarding their perspective on the progress IQ has made to date and the opportunities and challenges it faces moving forward.

In their remarks, all three emphasized the significance of the collaboration across companies that IQ has achieved, and the importance of continuing to build an environment which encourages companies to work together to develop solutions and provide improved patient care. Dr. Tougas and Dr. King spoke to the need to continue justifying the value of the Consortium by producing concrete deliverables and focusing on scientific output, while Dr. Kinter acknowledged that there is a need to further define what collaboration looks like in the pharmaceutical industry as this is a relatively new concept in the field. Each referenced the fact that success builds success, particularly in regard to data sharing, and that as companies see the benefit they derive from sharing data this will reduce the effort needed to do so in future projects.

To the questions of how to increase dialogue and collaboration across IQ Leadership Groups and how to increase the global impact of the IQ Consortium, Dr. King, Dr. Tougas, and Dr. Kinter recognized the need for a long-term strategy around these goals and the fact that the Consortium needs to continue to adapt to keep pace with changes in the industry and to maximize opportunities for success.

In closing, all three shared their vision for the IQ Consortium five to ten years from now, indicating IQ leadership, both past and present, would like to see this organization more proactively impacting both the academic and regulatory spheres, advancing the rate of drug development and decreasing attrition, better collaborating on science, and increasing the value delivered to all IQ stakeholders.

Breakout Session Reports

The afternoon of the Symposium was composed of breakout sessions and reports on those sessions. Participants discussed the topics that follow, and proposed ideas for addressing these questions. Key observations and recommendations from each session are presented below, as shared in the IQ Symposium Breakout Reports.

A: How to increase engagement and cross-functional collaboration in LGs/WGs?

- Increasing support from the Secretariat at all levels.
- Creating a training tool kit for WGs and LGs.
- Creating opportunities for dialogue across leadership groups (*e.g., CMC LG calls*).
- Creating awareness across LGs about new WGs to increase cross-pollination.

B: Impacting Regulatory Authorities within and outside of the US

- Leverage our database
  - For example, could we help to calibrate risk?
  - This is unique to IQ
  - Dialogue is easier with science and data
- Globalization
  - Strategically partnering with other consortia to leverage other regions or expertise
- IQ LGs and WGs need clear rules of engagement with other consortia, experts, and/or regulatory authorities
  - How do we empower LGs and WGs?

- **C: Innovative Development Approaches**
  - Step back to go forward. Do more failure analysis.
    - Support the IQ database development initiative
    - Identify venue(s) for publication and sharing of learnings
  - Support IQ initiatives that already do innovative research
    - Understand biology and target better before embarking on clinical trials, even if it takes more time.
    - Support and expand efforts like microphysiological systems (cross-LG with NIH) and quantitative systems pharmacology

D: Clinical Trials of the Future

- How can we change our approach?
  - Use of mobile health technologies, e.g. to measure adherence
  - Greater engagement of patients in trials and trial design
  - Shared clinical trial infrastructure: can we compete on the medicine and not on the infrastructure?
  - Collaborate to understand disease progression, and use that knowledge to inform drug development?
- Objective: We should seek to streamline and improve the rigor of clinical trials by…
  - Measuring new factors and advance knowledge of disease
  - Increasing quality and integrity of data from clinical trials
  - Increasing patient motivation and adherence
- Possibilities for IQ:
  - Develop framework approach for clinical trial information, to increase usability of data in multiple settings
    - What will we measure, and how?
    - How will we use the data?
      - Precompetitive, collaborative analysis
- Company-specific analysis

E: Outsourcing

- Issues with outsourcing are common across functional areas and disciplines
- Many IQ companies have the same ultimate "customer" –regulatory agencies – but different interpretations of what that "customer" wants.
- Where can IQ add value?
    - Develop a common understanding of regulatory expectations
    - Developing a "language" for quality aspects common across industry
    - Facilitate the creation of a forum where vendors and pharma can interact to address common concerns, possibly through engagement with another industry association
- Appropriate benchmarking activities to identify areas for collaborative activities
- Soliciting participation in a cross-functional exploratory working group to gauge interest in the topic

F. Application of Novel Technologies to Enhance Value of Early Development

- Overall theme: Need to identify major gaps/pain points across the Development enterprise
    - Reduce attrition rate
    - Reduce development cost/time
- Solutions to gaps may take different approaches
    - Seek current tech and apply
    - Drive development of Novel Tech
- Partnership Frameworks
    - LGs/WGs
    - Enabling Tech Consortium
    - Cross-consortium partnership
    - Need to be aware of potential duplication of effort

2015 Symposium Organizing Committee Members

Chair, Ingrid Mergelsberg, Merck & Co., Inc.

Co-chair, Dennis O'Connor, Boehringer Ingelheim Pharmaceuticals, Inc.

Volker Fischer, AbbVie Inc.

Elisabeth Mortimer, AstraZeneca Global R&D

James Hartke, Celgene Corporation

Noel Dybdal, Genentech, Inc

Robyn Rourick, Genentech, Inc

Karen Evans, GlaxoSmithKline PLC

David Christopher, Merck Research Laboratories

Trupti Dixit, Takeda Global Research & Development Center, Inc.

Piyush Patel, Teva Branded Pharmaceutical Products R&D

2015 Symposium Awards

Analytical Leadership Group	
Michael Jones, Pfizer	Co-lead, Impurities Control WG
Drug Metabolism Leadership Group	
Chris Evans, GSK	Co-lead, Microsampling Working Group
DruSafe Leadership Group	
Bill Bracken, AbbVie	FDA Draft Guidance on "Investigational Enzyme Replacement Therapy: Nonclinical Assessment."
Mazin Derzi, Pfizer	Co-lead on FDA Draft Guidance on "Rare Diseases: Common Issues in Drug Development" response collation
Lee Silverman, Agios	Co-lead on FDA Draft Guidance on "Rare Diseases: Common Issues in Drug Development" response collation
Kenjie Amemiya, Genentech	Organized (icw PhUSE and CDISC) an open meeting on SEND implementation at the 2015 SOT Annual Meeting
Kerry Blanchard, Boehringer Ingelheim	Organized (icw PhUSE and CDISC) an open meeting on SEND implementation at the 2015 SOT Annual Meeting
Rod Prell, Genentech	Presented on nonclinical immunostimulation models and the FDA internal workshop on Immuno-Oncology on reproductive toxicity testing of immune enhancing therapeutics 2015 joint FDA/DruSafe/BioSafe annual meeting
Doug Keller, Sanofi	Presented on current experience with in vitro microphysiology models 2015 joint FDA/DruSafe/BioSafe annual meeting and the NIH/NCATS workshop on microphysiology systems
Donna Dambach, Genentech	Organized (icw FDA and AACR) "Best Practices on Dose Finding of Small Molecule Oncology Drugs" Workshop
Mary Ellen McNerney, BMS	Lead on FDA Draft Guidance on "Assessment of Male-Mediated Development Risk for Pharmaceuticals" response collation
3Rs Leadership Group	
Letty Medina, AbbVie	Led development effort for special edition of a major laboratory animal focused publication (Journal of the American Association for Laboratory Science)

Our Mission: The IQ Consortium is dedicated to augmenting the capability of member companies to develop transformational solutions that benefit patients, regulators and the broader R&D community. We encourage you to visit IQ online at www.iqconsortium.org, or connect with IQ on LinkedIn.