Welcome to the CMC Strategy Forum
(July 20-21, 2016)

We are pleased to welcome you to the CMC Strategy Forum. The purpose of the CMC Strategy Forum is to provide a venue for biotechnology/biological product discussion. The meetings focus on relevant CMC issues throughout the lifecycle of a product and thereby foster collaborative technical and regulatory interactions. The Forum strives to share information with the regulatory agencies to assist them in merging good scientific and regulatory practices. Outcomes of the Forum meetings are published in an appropriate peer-reviewed journal.

Each meeting will focus on a CMC related issue such as product characterization, comparability, specifications, etc. The format of each meeting will consist of case studies and presentations by Industry and/or FDA experts to introduce the topic and the key issues of concern. Breakout sessions will then be conducted to allow for additional discussion on the technical and regulatory details of the topics. It is envisioned that the final outcome of the workshop discussions will be the development of a document to be submitted to the appropriate Regulatory Agency designees for their consideration in developing and/or clarifying good regulatory practice guidelines for biotechnology derived products.

The success of the CMC Strategy Forum will depend on your active participation in discussing and raising issues pertaining to development of biologics. We encourage you to participate wholeheartedly in the workshops that have been designed to stimulate exchange of ideas and information.

We would like to thank the speakers who are giving generously of their time and resources, and to you, for your attendance. We acknowledge the generosity of our program partners: AbbVie, Inc., Amgen Inc., Biogen, Eli Lilly and Company, F. Hoffmann-La Roche Ltd., Genentech, a Member of the Roche Group, Janssen Pharmaceutical R&D, LLC, MedImmune, a member of the AstraZeneca Group, Merck & Co., Inc., Novo Nordisk A/S and Pfizer Inc. We are grateful for the expert management from CASSS and the audio-visual expertise of Michael Johnstone from MJ Audio-Visual Productions. Their experience and guidance in the preparation of this Forum has been invaluable.
ACKNOWLEDGEMENTS

CMC STRATEGY FORUM NORTH AMERICA PROGRAM COMMITTEE

Siddharth Advant, Kemwell Biopharma
Yves Aubin, Health Canada
John Bishop, CBER, FDA
Barry Cherney, Amgen Inc.
JR Dobbins, Eli Lilly and Company
Julia Edwards, Biogen
Sarah Kennett, CDER, FDA
Joseph Kutza, MedImmune, A member of the AstraZeneca Group
Kimberly May, Merck & Co., Inc.
Anthony Mire-Sluis, AstraZeneca
Stefanie Pluschkell, Pfizer, Inc.
Nadine Ritter, Global Biotech Experts, LLC
Dieter Schmalzing, Genentech, a Member of the Roche Group
Timothy Schofield, GlaxoSmithKline
Zahra Shahrokh, ZDev Consulting
Jeffrey Staecker, BioPhia Consulting, Inc.
Andrew Weiskopf, Biogen
Marcel Zocher, Bristol-Myers Squibb Company

CMC STRATEGY FORUM GLOBAL STEERING COMMITTEE

Siddharth Advant, Kemwell Biopharma, USA
Daniela Cerqueria, ANVISA-Brasilian National Health Surveillance Agency, Brasil
John Dougherty, Eli Lilly and Company, USA
Yasuhiro Kishioka, PMDA-Pharmaceutical and Medical Devices Agency, Japan
Junichi Koga, Daiichi Sankyo Co., Ltd., Japan
Steven Kozlowski, CDER, FDA, USA
Ingrid Markovic, CBER, FDA, USA
Rohin Mhatre, Biogen, USA
Anthony Mire-Sluis, AstraZeneca, USA
Wassim Nashabeh, F. Hoffmann-La Roche Ltd., Switzerland (Chair)
Ilona Reischl, AGES-Austrian Medicines and Medical Devices Agency, Austria
Anthony Ridgway, Health Canada, Canada
Nadine Ritter, Global Biotech Experts, LLC, USA
Thomas Schreitmüller, F. Hoffmann-La Roche Ltd., Switzerland
Mark Schenerman, MedImmune, A member of the AstraZeneca Group, USA
Karin Sewerin, BioTech Development AB, Sweden
The Organizing Committee gratefully acknowledges the pharmaceutical and biotechnology industry for their generous support of the CMC Strategy Forum North America series:

**STRATEGIC DIAMOND PROGRAM PARTNER**

Genentech, a Member of the Roche Group

F. Hoffmann-La Roche Ltd.

**STRATEGIC PLATINUM PROGRAM PARTNER**

AbbVie, Inc.

Biogen

MedImmune, A member of the AstraZeneca Group

**STRATEGIC GOLD PROGRAM PARTNER**

Novo Nordisk A/S

**STRATEGIC SILVER PROGRAM PARTNER**

Merck & Co., Inc.

Pfizer, Inc.

**PROGRAM PARTNERS**

Amgen Inc.

Eli Lilly and Company

Janssen Pharmaceutical R & D, LLC
The Scientific Organizing Committee gratefully acknowledges the following media for their promotional consideration of CMC Strategy Forum North America July 2016:

**LEADING MEDIA PARTNERS**

**BioProcess International**
**International Pharmaceutical Quality**

**MEDIA PARTNERS**

**American Laboratory / LabCompare**
**American Pharmaceutical Review**
**Analyst / Analytical Methods**
**BioProcessing Journal**
**Royal Society of Chemistry**
**separationsNOW.com**
**Technology Networks**
**The Analytical Scientist**
**The Medicine Maker**
**The Pathologist**
Change Happens: Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management

FORUM CO-CHAIRS:
Julia Edwards, Biogen, USA
Joseph Kutza, MedImmune, A member of the AstraZeneca Group, USA
Emanuela Lacana, CDER, FDA, USA
Ingrid Markovic, CBER, FDA, USA

SCIENTIFIC ORGANIZING COMMITTEE:
Michael Abernathy, Amgen Inc., USA
Sally Anliker, Eli Lilly and Company, USA
Yves Aubin, Health Canada, Canada
Michelle Frazier, AbbVie, Inc., USA
Markus Goese, F. Hoffmann-La Roche Ltd., Switzerland
Frank Montgomery, AstraZeneca, United Kingdom

In the current global regulatory environment, the management of post-approval CMC changes is often unpredictable and inefficient. Timelines for change approval can vary, from months to years, depending on regional regulatory timelines. Therefore, in post-approval lifecycle management, the challenge is to maintain a constant supply of high quality product while supporting innovation and continual improvement. The purpose of this forum is to explore pathways for operational flexibility in the post-approval phase of the product lifecycle. Case studies will be illustrated with specific examples that leverage ICH Q8, Q9, Q10, and Q11 concepts, which drive toward globally consistent management of post-approval changes. In close alignment with ongoing work on ICH Q12, the forum will highlight the benefits of clearly defining established conditions (i.e., regulatory commitments), further reliance of Pharmaceutical Quality System (PQS), post-approval change management protocols, and the level of detail provided to support a change that ensures sufficient manufacturing flexibility.

The questions this CMC Strategy Forum will answer:

1. What current or future regulatory pathways or tools would provide global operational flexibility in making post-approval changes? Does this look different for accelerated programs?
2. What are the benefits, challenges, and tradeoffs associated with leveraging these pathways and tools?
3. How do we close the gap between approval timelines (and data requirements) for post-licensure changes between ICH and non-ICH countries?
## CMC Strategy Forum Program Summary

### Change Happens: Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management

**Wednesday, July 20, 2016**

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>07:30 – 17:00</td>
<td><strong>Registration</strong> in the Washingtonian Ballroom Foyer</td>
</tr>
<tr>
<td>07:30 – 08:30</td>
<td><strong>Breakfast</strong> in the Washingtonian Ballroom Foyer</td>
</tr>
<tr>
<td>08:30 – 08:45</td>
<td><strong>CASSS Welcome and Introductory Comments</strong> in Salons D - G</td>
</tr>
<tr>
<td></td>
<td>Wassim Nashabeh, <em>F. Hoffmann-La Roche Ltd.</em></td>
</tr>
<tr>
<td></td>
<td><strong>CMC Strategy Forum Welcome and Introductory Comments</strong> in Salons D - G</td>
</tr>
<tr>
<td></td>
<td>Julia Edwards, <em>Biogen</em></td>
</tr>
<tr>
<td></td>
<td>Joseph Kutza, <em>MedImmune, A member of the AstraZeneca Group</em></td>
</tr>
</tbody>
</table>

### “The Problem Statement”

**Workshop Session One** in Salons D - G  
**Session Chairs:** Yves Aubin, *Health Canada* and Joseph Kutza, *MedImmune, A member of the AstraZeneca Group*

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
</table>
| 08:45 – 09:15 | **An Industry Perspective: The Complexity of Post-approval CMC Changes and Proposed Regulatory Strategies**  
Suzanne Murray, *Biogen (representing Biophorum Operations Group (BPOG), United Kingdom)* |
| 09:15 – 09:45 | **Challenges Posed by Post Approval Changes on a Commercial Biologic: A Manufacturing and Supply Chain Perspective**  
Randall Lapcevich, *MedImmune, A member of the AstraZeneca Group, Gaithersburg, MD USA* |
| 09:45 – 10:15 | **Managing the Product Lifecycle Continuum through Post-approval Change Management Plans: An Industry Perspective**  
Gresham Weatherly, *AbbVie, Inc., North Chicago, IL USA* |
| 10:15 – 10:45 | **Networking Break** in the Washingtonian Ballroom Foyer                                    |
| 10:45 – 12:00 | **PANEL DISCUSSION – Questions and Answers**  
Randy Lapcevich, *MedImmune, A member of the AstraZeneca Group, USA*  
Anthony Mire-Sluis, *AstraZeneca, USA*  
Suzanne Murray, *Biogen (representing Biophorum Operations Group (BPOG), United Kingdom)*  
Anthony Ridgway, *Health Canada, Canada*  
Anders Vinther, *Sanofi Pasteur, USA*  
Gresham Weatherly, *AbbVie, Inc., USA* |
Wednesday, July 20 continued…

12:00 – 13:30  **Networking Lunch** in the Washingtonian Ballroom Foyer

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>12:00 – 13:30</td>
<td>Networking Lunch in the Washingtonian Ballroom Foyer</td>
</tr>
<tr>
<td>14:20 – 14:45</td>
<td><strong>ICH Q12: A Much Needed Culture Shift</strong> Mahesh Ramanadham, CDER, FDA, Silver Spring, MD USA</td>
</tr>
<tr>
<td>14:45 – 15:10</td>
<td><strong>Post-approval Changes in Japan</strong> Yasuhiro Kishioka, Pharmaceuticals and Medical Devices Agency (PMDA), Tokyo, Japan</td>
</tr>
<tr>
<td>15:15 – 15:45</td>
<td><strong>Networking Break</strong> in the Washingtonian Ballroom Foyer</td>
</tr>
<tr>
<td>15:45 – 17:00</td>
<td><strong>PANEL DISCUSSION – Questions and Answers</strong> Yasuhiro Kishioka, Pharmaceuticals and Medical Devices Agency (PMDA), Japan Wassim Nashabeh, F. Hoffmann-La Roche Ltd., Switzerland Mahesh Ramanadham, CDER, FDA, USA Anthony Ridgway, Health Canada, Canada Patrick Swann, Biogen, USA</td>
</tr>
<tr>
<td>17:00 – 18:30</td>
<td><strong>Networking Reception</strong> in the Washingtonian Ballroom Foyer</td>
</tr>
<tr>
<td>18:30</td>
<td><strong>Adjourn Day One</strong></td>
</tr>
</tbody>
</table>
Thursday, July 21, 2016

08:00 – 17:00  
**Registration** in the Washingtonian Ballroom Foyer

07:45 – 08:45  
**Breakfast** in the Washingtonian Ballroom Foyer

<table>
<thead>
<tr>
<th>Time</th>
<th>Session Description</th>
</tr>
</thead>
</table>
| 08:45 – 09:15 | **FDA Perspectives on Established Conditions and ICH Q12**  
ASHLEY BOAM, CDER, FDA, Silver Spring, MD USA |
| 09:15 – 09:45 | **Complexities of CMC Change Management and Q12 Opportunities**  
JAMES SESIC, AMGEN INC., THOUSAND OAKS, CA USA |
| 09:45 – 10:15 | **20/20 Vision: Predicting the Future of ICH Q12 in Practice**  
KIMBERLY WOLFRAM, BIOGEN, CAMBRIDGE, MA USA |
| 10:15 – 10:45 | **Networking Break** in the Washingtonian Ballroom Foyer                                                   |
| 10:45 – 12:00 | **PANEL DISCUSSION – Questions and Answers**  
SALLY ANLIKER, ELI LILLY AND COMPANY, USA  
ASHLEY BOAM, CDER, FDA, USA  
JENNIFER MERCER, GENENTECH, A MEMBER OF THE ROCHE GROUP, USA  
JAMES SESIC, AMGEN INC., USA  
KIMBERLY WOLFRAM, BIOGEN, CAMBRIDGE, MA USA |
| 12:00 – 13:30 | **Networking Lunch** in the Washingtonian Ballroom Foyer                                                  |

<table>
<thead>
<tr>
<th>Time</th>
<th>Session Description</th>
</tr>
</thead>
</table>
| 13:30 – 14:00 | **Improving Post-approval Change Processes as a Way to Ensure Technical Innovation and Drug Product Availability**  
ANDERS VINTHER, SANOFI PASTEUR, SWIFTWATER, PA USA |
| 14:00 – 14:30 | **The Device Side of Combination Products: Technical and Regulatory Challenges in Life Cycle Management**  
ROBERT LAUGNHER, MEDEMMUNE, A MEMBER OF THE ASTRAZENECA GROUP, GAITHERSBURG, MD USA |
| 14:30 – 15:00 | **The Potential Benefits and Challenges of ICH Q12 for Managing Global Changes**  
JENNIFER MERCER, GENENTECH, A MEMBER OF THE ROCHE GROUP, SOUTH SAN FRANCISCO, CA USA |
| 15:00 – 15:30 | **Networking Break** in the Washingtonian Ballroom Foyer                                                  |
Thursday, July 21 continued…

15:45 – 17:00  **PANEL DISCUSSION – Questions and Answers**
Monica Bernardes Floreano, *ANVISA-Brazilian Health Surveillance Agency, Brasil*
Robert Iser, *CDER, FDA, USA*
Robert Laughner, *MedImmune, A member of the AstraZeneca Group, USA*
Jennifer Mercer, *Genentech, a Member of the Roche Group, USA*
Suzanne Murray, *Biogen, USA*
Anders Vinther, *Sanofi Pasteur, USA*

17:00 – 17:30  **Recap of Program**
Summary Slide Presentation
Demetra Macheras, *AbbVie, Inc.*
Kimberly Wolfram, *Biogen*

17:30 – 17:45  **Invitation to CMC Strategy Forum January 2017**

17:45  **Adjournment**
After approval of a biologic product it is business as usual to make changes such as increased batch sizes and new manufacturing facilities to expand patient access. Additional changes are often made to improve process robustness and yield or to improve analytical methods as companies gain experience in commercial manufacture and testing. Changes may also be made to comply with new regulatory expectations. Before changes are made, risks to the process are evaluated and data are generated to confirm that there is no adverse impact to product quality. As a result of global regulatory requirements, many changes cannot be implemented until regulatory agency review and approval which can take several years in the case of a change that needs to be implemented globally. The same core data and information may be reviewed by up to 140 countries according to local procedures and timelines. Health authorities often have questions during reviews, leading to preparation of many rounds of responses simultaneously. Multiple reviews of the same information, does not improve safety, quality or efficacy and may lead to higher costs, a more complex supply chain, and a need for sophisticated systems to maintain regulatory compliance. ICH and WHO efforts, while appreciated, are limited, not always aligned, and not applied globally. This session will explore the core concerns associated with the current overly complex global system with an eye towards potential solutions.

NOTES:
Randall Lapcevich
*MedImmune, A member of the AstraZeneca Group*

Randy Lapcevich has been working in the biopharmaceuticals industry for 25 years and is currently a global supply director, AstraZeneca Global Biologics Operations division, responsible for end-to-end supply and life-cycle management for Synagis®. Synagis® is a commercial biologic approved in the US and 84 ROW countries developed to treat Respiratory Syncytial Virus. Areas of leadership include strategic and tactical management of cross-site functional teams responsible for the manufacture, validation, testing and shipment of commercial product as well as external manufacturing support and coordination of regulatory and supply chain strategies with internal and external manufacturing planning.

Since joining AstraZeneca/MedImmune in 2005, Randy has held positions in bio-process development where he led a group responsible for technology transfers and tech support of clinical and commercial products as well as providing oversight of a scale-up laboratory responsible for producing pre-clinical material and purification process scale-up development. Prior to joining AstraZeneca, Randy obtained extensive experience in biologics process development, protein purification, project management and a short stint working in discovery research. He is an author on two US patents and received a bachelor’s degree in cellular and molecular biology from West Virginia University.

Anthony Mire-Sluis
*AstraZeneca*

Suzanne Murray
*Biogen (representing Biophorum Operations Group (BPOG))*

Sue Murray is a senior director of regulatory affairs, CMC at Biogen based in Cambridge, MA. Sue has been at Biogen for 12 years and is currently responsible for global regulatory CMC strategy. She manages a regulatory team responsible for regulatory CMC global emerging markets, outsourcing and compliance. During her tenure at Biogen, Sue has held numerous roles within the regulatory and quality organizations. Sue is an active member in industry groups and will represent the Biophorum Operations Group (BPOG) at the CMC Strategy Forum. Sue holds a BS and MS in chemical engineering from the University of Massachusetts, Lowell.

Anthony Ridgway
*Health Canada*

Dr. Ridgway completed his PhD at McGill University in Montreal, and then proceeded to post-doctoral studies followed by an assistant professorship in the Cancer Research Laboratory and Department of Microbiology and Immunology at the University of Western Ontario. Academic research activities included work on the structure and expression of oncogenes, retroviral and HIV regulatory elements and inducible expression vectors. He has been with Health Canada since 1991 and in 1999, became manager of the biotherapeutics division, with responsibility for regulation of a wide range of products. In 2004, he guided the separation of his former division into three new divisions and became the senior
regulatory scientist in the office of the director in the newly formed Centre for Evaluation of Radiopharmaceuticals and Biotherapeutics, BGTD. He holds a range of advisory and supervisory responsibilities that includes retaining managerial responsibility for the evaluation of product quality for radiopharmaceuticals and gene therapy products. He has been active with the ICH* since 1993, serving on Expert Working Groups addressing the quality of biotechnology products and is currently with Q12. He has been active on consecutive US Pharmacopoeia Committees of Experts, since June 2000. Dr. Ridgway has been extensively involved in the Canadian approach to subsequent-entry biologics (biosimilars), and the drafting and dissemination of Canadian guidance.

*International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use

**Anders Vinther**
*Sanofi Pasteur*

Anders Vinther is chief quality officer at the vaccine company Sanofi Pasteur. He has a MSc and PhD in chemical engineering from the Technical University of Denmark. Anders has worked in many different cultures and has experience from both small and large companies. He was the co-founder of the contract manufacturing organization CMC Biologics, VP of quality in Novo Nordisk, and most recently before joining Sanofi Pasteur he was VP of quality for Genentech and Roche Biologics product operations. Anders is the past chairman of Parenteral Drug Association (PDA), and is a quality thought leader currently working on the Living Quality Ecosystem as well as ways to achieve sustainable quality. Outside his work in the pharma industry Anders is the owner and winemaker at Flying Suitcase Wines.

**Gresham Weatherly**
*AbbVie, Inc.*

Gresham Weatherly received his PhD in chemistry from the University of North Carolina studying protein-protein interactions. After graduate school, he worked for a contract biologic manufacturer doing downstream process development and manufacturing support for early phase clinical products. He then moved to Worcester, MA to work for Abbott continuing to work on downstream process development/manufacturing support for biological products. After ten years of process development, Gresham transferred to CMC Regulatory Affairs in Abbott working on biologic products including filing post-approval changes for Humira.
Pharmaceutical products save or improve the lives of millions of people throughout the world each year. While thorough regulatory review of Chemistry, Manufacturing and Controls (CMC) information is critical to ensure the safety, quality and efficacy, patients’ quick access to the products is hindered by lack of collaboration among regulators, lack of harmonization in the requirements and extensive review times. Companies race to launch products to patients as soon as possible after clinical efficacy is demonstrated and often, changes such as increased batch sizes and new manufacturing facilities are needed to expand patient access. Additional changes are often made to improve product quality or process robustness as companies gain experience in commercial manufacture.

There is tremendous variability in review and approval times for changes in each market, with some markets taking more than 4 years while others approve in a month. Over the course of 4 years, while one country may only approve a single change, another country may approve two dozen. The same core data and information may be reviewed over and over again by approximately 140 individual regulatory bodies according to 140 separate timelines, which dramatically increases the potential for errors in regulatory compliance, complexity in managing inventory, manufacturing costs and risk of interruptions of the product supply to patients. Alternate regulatory strategies are proposed to enable quicker review, approval, and implementation times so that patients can have fast access to high quality products manufactured at the lowest possible costs.
Challenges Posed by Post Approval Changes on a Commercial Biologic: A Manufacturing and Supply Chain Perspective

Randall Lapcevich

MedImmune, A member of the AstraZeneca Group, Gaithersburg, MD USA

With increased competition in the biopharma space to commercialize new molecular entities in the least amount of time possible, the product development, process validation and launch timelines have been truncated dramatically. This time-crunch has forced the Development and Supply Chain organizations to find creative ways of addressing the additional risks that are created by this situation. One of the outputs from this constrained schedule is that several process and product related improvements need to be addressed after launch through the Post Approval Change process. The lack of continuity around the approval timing and requirements from region-to-region around the globe place a tremendous challenge on Supply Chain to successfully meet product demand while managing risks around inventory, manufacturing and obsolescence. Any progress we can make towards addressing the disparities in approval timeframe and requirement expectation will remove or reduce some of the risks and challenges that Supply Chain organizations are facing as part of commercial life-cycle management.

Slides were not available at the time of printing.

NOTES:
Managing post-approval changes for globally approved products is cumbersome and can take several years to receive approval globally. While a change is being submitted and reviewed by many regulatory agencies, other changes continue to be evaluated that results in several staggered changes being managed through global approvals. This complexity is difficult to manage, may limit innovation, or result in different product supply chains per market. The use of change management plans can reduce the regulatory complexity and give certainty to change protocols and timelines in ICH markets. However, most of the regulatory complexity and uncertainty is from non-ICH countries. An ideal state for lifecycle management would have change plans approved in global marketing authorizations that would allow change management be conducted within the Quality system, and if required, submitted after implementation.

NOTES:
Panel Discussion – Questions and Answers
Randy Lapcevich, MedImmune, A member of the AstraZeneca Group, USA
Anthony Mire-Sluis, AstraZeneca, USA
Suzanne Murray, Biogen (representing Biophorum Operations Group (BPOG), United Kingdom)
Anthony Ridgway, Health Canada, Canada
Anders Vinther, Sanofi Pasteur, USA
Gresham Weatherly, AbbVie, Inc., USA

The following questions will guide the panel discussion:

1. How does your organization manage post-approval changes to minimize the number of “flavors” that need to be manufactured and to minimize compliance issues?

2. Based on what you have seen so far, is ICH Q12 going far enough to address the most critical issues associated with post-approval change management? If not, what is missing? Any proposed edits?

3. Given that a single post-approval change of a relatively minor nature can take 3-5 years to implement globally, how can regulatory agencies within and beyond ICH countries work together to address significant challenge to supplying patients with products using the most up-to-date manufacturing processes and sites?

NOTES:
Session Chairs: Sally Anliker, *Eli Lilly and Company* and Emanuela Lacana, *CDER, FDA*

This session will provide an overview of the status of ICH Q12 from the perspective of both global regulators and industry. The opportunities and challenges will be shared from several vantage points. Further, the linkage between regional advancements in lifecycle management such as FDA's new draft guideline on established conditions and the broader global harmonization effort will be elucidated.

NOTES:
Yasuhiro Kishioka
*Pharmaceuticals and Medical Devices Agency (PMDA)*

Dr. Kishioka is a principal reviewer in the Office of Cellular and Tissue-based Products of the Japanese regulatory agency, Pharmaceuticals and Medical Devices Agency (PMDA). Since joining PMDA in 2008, his main work is the pharmaceutical quality review of biotechnological/biological products. His areas of expertise also include biosimilars and he has been assigned as the ICH Q12 topic leader of Japanese regulatory authorities. He holds a PhD from Hokkaido University in meat science with emphasis in molecular biology.

Wassim Nashabeh
*F. Hoffmann-La Roche Ltd.*

Dr. Wassim Nashabeh received his PhD in analytical chemistry from Oklahoma State University in 1993, and his post-doctoral fellowship in bioanalytical chemistry from The Barnett Institute at Northeastern University. Following a two-year research appointment at PerSeptive Biosystems, Wassim joined Genentech (*A member of the Roche Group*) in 1996 as a scientist and has since held several positions of increasing responsibilities including associate director of the methods validation group, director quality control, director in the CMC regulatory affairs group, senior director of CMC policy & strategy, global head of technical regulatory policy for the Roche Pharma Medicines Group and most recently as the global head of policy and international operations in PTR. His current responsibilities include development and advocacy of Roche key external positions and policies with global health authorities, industry associations and scientific organizations, as well as management of Roche technical regulatory international operations.

Mahesh Ramanadham
*CDER, FDA*

Anthony Ridgway
*Health Canada*

Dr. Ridgway completed his PhD at McGill University in Montreal, and then proceeded to post-doctoral studies followed by an assistant professorship in the Cancer Research Laboratory and Department of Microbiology and Immunology at the University of Western Ontario. Academic research activities included work on the structure and expression of oncogenes, retroviral and HIV regulatory elements and inducible expression vectors. He has been with Health Canada since 1991 and in 1999, became manager of the biotherapeutics division, with responsibility for regulation of a wide range of products. In 2004, he guided the separation of his former division into three new divisions and became the senior regulatory scientist in the office of the director in the newly formed Centre for Evaluation of Radiopharmaceuticals and Biotherapeutics, BGTD. He holds a range of advisory and supervisory responsibilities that includes retaining managerial responsibility for the evaluation of product quality for radiopharmaceuticals and gene therapy products. He has been active with the ICH* since 1993, serving on Expert Working Groups addressing the quality of biotechnology products and is currently with Q12.
He has been active on consecutive US Pharmacopoeia Committees of Experts, since June 2000. Dr. Ridgway has been extensively involved in the Canadian approach to subsequent-entry biologics (biosimilars), and the drafting and dissemination of Canadian guidance.

*International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use

**Patrick Swann**

*Biogen*

Patrick Swann is currently a senior director in the CMC regulatory affairs group at Biogen where his is responsible for providing cross-program strategic CMC regulatory direction to Biogen programs and pharmaceutical operations & technology initiatives (e.g. Quality by Design, Advanced Process Controls). Prior to his current role, he led the analytical development group which was responsible for developing and implementing bioassay and biochemical methods that directly support multiple preclinical and clinical programs. From 1998 to 2013, he worked at US FDA where he was the deputy director of the division of monoclonal antibodies and also served as the biotechnology product representative for FDA on the ICH Q11 expert working group. He has given numerous presentations and authored or co-authored several publications on analytical methods and biotechnology product development and manufacture.
Regulatory Guidance for Product Lifecycle Management: Harmonization Goals, Opportunities and Challenges

Anthony Ridgway

Health Canada, Ottawa, ON Canada

A perspective will be provided on the aspirations, issues, challenges and opportunities associated with development of the ICH Q12 guideline. Elements will include: the enduring value of risk-rationalized categorization of manufacturing changes requiring communication with the regulator; “regulatory commitments” or “established conditions” and their potential for leveraging “regulatory relief”; a possible new life for post-approval change management protocols; and the potential for Q12 to have significant value beyond current ICH jurisdictions through “ICH-independent” harmonization and regulatory convergence.

NOTES:
Will ICH Q12 Truly Go Beyond Q8/11? Opportunities and Challenges

Wassim Nashabeh

F. Hoffmann-La Roche Ltd., Basel, Switzerland

This presentation will focus on the current challenges and opportunities facing the development of ICH Q12, the first ICH Q document solely focused on post-approval changes for pharmaceuticals. Q12 is seen as a continuation of the ICH Quality vision that started with Q8 continuing through Q11. Q12 can potentially hold the promise of bringing meaningful and pragmatic benefits following implementation, something that has not yet been truly realized yet through implementation of Q8/11, so that the original promise of the ICH Quality vision can be realized. The newly introduced concept of established conditions will be discussed from a pragmatic perspective including examples of how such conditions could be selected for a biologic, and be linked to knowledge and risk calibration.

NOTES:
ICH Q12: A Much Needed Culture Shift

Mahesh Ramanadham

*CDER, FDA, Silver Spring, MD USA*

Abstract was not available at the time of printing.

NOTES:
Post-approval CMC Changes in Japan: How We Envision the Future

Yasuhiro Kishioka

Pharmaceuticals and Medical Devices Agency (PMDA), Tokyo, Japan

In Japan, the Application Form (AF) found in Module 1.2 is submitted to PMDA together with ICH Common Technical Document (CTD) at the time of application for marketing authorization. When a product is approved by the Minister of Health, Labor and Welfare, the AF becomes the legally binding document and a post-approval regulatory action is required if the marketing authorization holder changes the description in the AF (or Approved Matter; AM). Post-approval change reporting categories are also clarified in AF and these AMs are determined on a product-by-product basis, leading to the transparency and flexibility in terms of post-approval changes.

This presentation will provide the current perspectives on the post-approval CMC changes in Japan in connection with ICH Q12.

NOTES:
Changing How We Make Change: ICH Q12 Global Status and Impact Workshop Session Two

Panel Discussion – Questions and Answers
Yasuhiro Kishioka, Pharmaceuticals and Medical Devices Agency (PMDA), Japan
Wassim Nashabeh, F. Hoffmann-La Roche Ltd., Switzerland
Mahesh Ramanadham, CDER, FDA, USA
Anthony Ridgway, Health Canada, Canada
Patrick Swann, Biogen, USA

The following questions will guide the panel discussion:

1. How can we leverage ICH Q12 to focus global post-approval reporting on changes that really matter to patients?
   a. How will the concept of established conditions have an impact on lifecycle management and post approval change?
   b. What is the role of lifecycle management plans in the overall construct of ICHQ12?
   c. What opportunities can industry pursue to expand the use of protocols to ensure more effective and meaningful change submissions?

2. ICH countries are one part of the overall challenge associated with lifecycle management. How can we ensure that ICH Q12 works globally to develop risk-based post-approval reporting and to drive acceptance of pathways such as protocols and established conditions?

3. How will legacy products benefit from ICH Q12? What are the challenges for these products?

NOTES:
Session Chairs: Julia Edwards, Biogen and Ingrid Markovic, CDER, FDA

The policies and ideas introduced in the morning session are the first step in the industry's evolution toward more effective post-approval change management. However, this is the first step. How the concepts are implemented in practice by industry and received by regulators on a regional level is the next. This session will provide an overview of practical cases of how the ICHQ12 ideas may be implemented by industry in practice. Active dialogue with global regulators on the acceptability of these practical issues will drive toward a true revolution in post-approval change management that truly benefits patients and improves access.

NOTES:
**Sally Anliker**  
*Eli Lilly and Company*

**Ashley Boam**  
*CDER, FDA*

Ashley Boam currently serves as acting director of the Office of Policy for Pharmaceutical Quality (OPPQ) in the Office of Pharmaceutical Quality (OPQ) in the Center for Drug Evaluation and Research (CDER). OPPQ is responsible for developing and clearly communicating science, and risk-based policies and standards related to drug product quality, including application review and inspection. This Office also coordinates OPQ’s work with international regulatory authorities on quality issues, leads CDER’s compendial operations, coordinates CDER’s involvement in quality standard-setting organizations, and addresses policy issues related to drug-device combination products.

Prior to joining CDER, Ashley spent nearly 20 years in the Office of Device Evaluation (ODE) in FDA’s Center for Devices and Radiological Health (CDRH), serving as a scientific reviewer, a branch chief in the Division of Cardiology Devices, and finally as associate director for regulations and guidance for ODE. Ashley received her MSBE from the University of Alabama at Birmingham and her BSE from Tulane University, both in biomedical engineering.

**Jennifer Mercer**  
*Genentech, a Member of the Roche Group*

Jennifer Mercer is a senior director in regulatory CMC at Genentech (a member of the Roche Group) and has management responsibility for early and late stage clinical development products. She has nearly 30 years of experience in the biotech/pharmaceutical industry in multiple disciplines, including manufacturing, manufacturing sciences, cell culture process development, and regulatory affairs. She rejoined Genentech in late 2011 as a director of combination products, regulatory CMC and prior to that, she worked at Amgen (Thousand Oaks, CA) for 15 years in various positions and responsibilities in manufacturing, clinical regulatory affairs and regulatory CMC. She holds a BS in microbiology.

**James Sesic**  
*Amgen Inc.*

**Kimberly Wolfram**  
*Biogen*

Kim Wolfram is an associate director in regulatory affairs at Biogen Inc, based in Cambridge, MA. She is responsible for global regulatory strategy and has supported clinical, license, and post-marketing regulatory applications for biological and combination products. She is primarily dedicated to advancing late stage clinical products and developing strategies for novel manufacturing technologies. Kim is a member of the PhRMA ICH Q12 LD KIT. Prior to Biogen, she was in quality assurance at Abbott Bioresearch Center (now AbbVie), where she supported the contract manufacturing for Seattle Genetics and Zymogenetics. Kim received her MS degree in regulatory affairs and health policy from the Massachusetts College of Pharmacy and Health Sciences and an undergraduate degree in natural sciences from Saint Anselm College.
FDA Perspectives on Established Conditions and ICH Q12

Ashley Boam

CDER, FDA, Silver Spring, MD USA

Slides were not available at the time of printing.

NOTES:
Complexities of CMC Change Management and Q12 Opportunities

James Sesic

Amgen Inc., Thousand Oaks, CA USA

Throughout the commercial lifecycle, Biopharmaceutical companies need to implement hundreds of Manufacturing and Quality Control changes per year, to ensure an efficient and reliable supply of high quality products. Most changes are managed within the GMP Quality Management System and not subject to reporting to regulatory authorities prior to implementation. Nevertheless the small percentage of reportable changes require significant investment of resources from Industry to manage implementation in a compliant manner without interruption of supply. This presentation will describe some of the strategies employed by companies to manage this complexity, and review some of the opportunities and potential challenges associated with ICH Q12.

Slides were not available at the time of printing.

NOTES:
Compliant and flexible life cycle management is exceedingly important for the therapies of tomorrow. The promise of these disease modifying medicines combined with novel technologies will require robust control and post-approval adaptability. This presentation will take a journey to the future and imagine the realities of implementing ICH Q12 in the year 2020. From this vantage point, one can gain clarity and insights into the critical importance of optimizing life cycle management.

NOTES:
PANEL DISCUSSION – Questions and Answers
Sally Anliker, Eli Lilly and Company, USA
Ashley Boam, CDER, FDA, USA
Jennifer Mercer, Genentech, a Member of the Roche Group, USA
James Sesic, Amgen Inc., USA
Kimberly Wolfram, Biogen, Cambridge, MA USA

The following questions will guide the panel discussion:

Established Conditions
1. How will ECs help reduce regulatory burden associated with post-approval changes? Will this apply to all cases? For example, setting ECs with limited process/product knowledge early in development could result in tight ranges that require loosening with more knowledge. How will these instances be facilitated?
2. How can routine monitoring and verification be leveraged to maintain ECs over the product lifecycle?
3. How does performance-based approach to ECs compare to QbD? Are ECs just re-designing design space? Isn’t generating the produces/product knowledge needed to define ECs the same as what is done for QbD?
4. Can established conditions be leveraged for currently marketed products? How do you enable ECs for products that are currently in the market? Will ECs be beneficial in these cases?
5. What should be considered in cases where advanced/enhanced process controls are proposed?

Protocols
1. How can broad protocols be leveraged effectively to change specifications, for example. Can multiple changes be accounted for within a single protocol to facilitate global change?
2. Is there an opportunity to standardize approaches across classes of molecules such that we can push towards more global efficiency?
3. What elements of ICH Q12 do we already do globally? As an example, post-approval stability protocols are accepted globally even though there isn't an official 'protocol' in the submission.

NOTES:
The Holy Grail for any pharmaceutical company is a single, core marketing application dossier. ICH Q12 holds great promise in ICH countries, where a single set of registered conditions and post-approval change management plans will speed implementation and ease the burden of change control. However, considerable challenge remains in countries that have not yet adapted ICH principles. In these regions, lack of a unified approach and country-specific requirements hinder timely global change implementation and detract from what is gained with ICH-participating countries. The ability to leverage the proposed benefits from ICH Q12 can improve life-cycle consistency for non-ICH regions due to increased availability and continuous improvement of existing therapies. This session will focus on the above-mentioned challenges.

NOTES:
Robert Iser  
*CDER, FDA*

Bob joined the FDA in 2003. He is currently the acting director of the office of process & facilities (OPF), a part of the new office of pharmaceutical quality (OPQ). Prior to the formation of OPQ, Bob was acting associate director for policy development in the office of pharmaceutical science. He was also a division director and CMC team leader in the office of generic drugs. Prior to joining the FDA, Bob spent seven years in the pharmaceutical industry with industrial experience related to management of quality systems, analytical method development, and support of manufacturing process development, scale-up and validation.

Monica Bernardes Floreano  
*ANVISA-Brazilian Health Surveillance Agency*

Robert Laughner  
*MedImmune A member of the AstraZeneca Group*

Jennifer Mercer  
*Genentech, a Member of the Roche Group*

Jennifer Mercer is a senior director in regulatory CMC at Genentech (a member of the Roche Group) and has management responsibility for early and late stage clinical development products. She has nearly 30 years of experience in the biotech/pharmaceutical industry in multiple disciplines, including manufacturing, manufacturing sciences, cell culture process development, and regulatory affairs. She re-joined Genentech in late 2011 as a director of combination products, regulatory CMC and prior to that, she worked at Amgen (Thousand Oaks, CA) for 15 years in various positions and responsibilities in manufacturing, clinical regulatory affairs and regulatory CMC. She holds a BS in microbiology.

Suzanne Murray  
*Biogen*

Sue Murray is a senior director of regulatory affairs, CMC at Biogen based in Cambridge, MA. Sue has been at Biogen for 12 years and is currently responsible for global regulatory CMC strategy. She manages a regulatory team responsible for regulatory CMC global emerging markets, outsourcing and compliance. During her tenure at Biogen, Sue has held numerous roles within the regulatory and quality organizations. Sue holds a BS and MS in chemical engineering from the University of Massachusetts, Lowell.

Anders Vinther  
*Sanofi Pasteur*

Anders Vinther is chief quality officer at the vaccine company Sanofi Pasteur. He has a MSc and PhD in chemical engineering from the Technical University of Denmark. Anders has worked in many different cultures and has experience from both small and large companies. He was the co-founder of the contract manufacturing organization CMC Biologics, VP of quality in Novo Nordisk, and most recently before
joining Sanofi Pasteur he was VP of quality for Genentech and Roche Biologics product operations. Anders is the past chairman of Parenteral Drug Association (PDA), and is a quality thought leader currently working on the Living Quality Ecosystem as well as ways to achieve sustainable quality. Outside his work in the pharma industry Anders is the owner and winemaker at Flying Suitcase Wines.
Improving Post-approval Change Processes as a Way to Ensure Technical Innovation and Drug Product Availability

Anders Vinther

Sanofi Pasteur, Swiftwater, PA USA

The ICH Q10 objective of continual improvement including innovation seems to be happening at a slower pace than what many companies would prefer for various reasons. Variations in regulatory processes vary between various countries in terms of requirements and timelines, which leads to a logistics challenge for companies having to manage several product versions at the same time. This in turn increases risk to product availability. If we continue and expand the dialog between industry and regulators we have an opportunity to facilitate more innovation and improve drug product availability. The solution includes reduced regulatory filing submission burden and a strong science and risk based approach to post approval changes.

NOTES:
Combination products represent a growing part of many company’s portfolios. While the recognition of the challenges inherent to drug/device combination products by regulators and industry globally has increased greatly in recent years, there is still much work to be done to clarify expectations for many aspects of the development and regulation of these products. The management of post-approval changes to a combination product as part of its lifecycle management is one of those aspects. This presentation will focus on the challenges in implementing post-approval changes to the device aspects of a combination product. Addressing these challenges from a technical perspective will be covered with an eye towards compliance with FDA’s Quality System Regulations and ISO 13485. The challenges of managing the regulatory submission of these changes will be discussed both from a US and OUS perspective. Finally, current initiatives to improve clarity around these technical and regulatory challenges will be discussed.”

Slides were not available at the time of printing.

NOTES:
The Potential Benefits and Challenges of ICH Q12 for Managing Global Changes

Jennifer Mercer

*Genentech, a Member of the Roche Group, South San Francisco, CA USA*

Abstract was not available at the time of printing.

Slides were not available at the time of printing.

NOTES:
Panel Discussion – Questions and Answers
Monica Bernardes Floreano, ANVISA-Brazilian Health Surveillance Agency, Brasil
Robert Iser, CDER, FDA, USA
Robert Laughner, MedImmune, A member of the AstraZeneca Group, USA
Jennifer Mercer, Genentech, a Member of the Roche Group, USA
Suzanne Murray, Biogen, USA
Anders Vinther, Sanofi Pasteur, USA

The following questions will guide the panel discussion:

1. One of the major tenants of ICH Q12 is the concept of Established Conditions. These established conditions would be legally binding information and any changes would require prior approval from health authorities.
   a. What is the “right” balance for registered established conditions that meet health authority expectations yet allow for reasonable life-cycle management activities?
   b. How will companies achieve this balance and how can ICH Q12 aid in this activity?
   c. Will ICH Q12 provide additional clarity pertaining to the details expected in the regulatory filing in comparison to those presented during inspection?

2. In theory, ICH Q12 has the potential to benefit regulators, industry, and patients by streamlining implementation of post-approval changes.
   a. How can ICH Q12 facilitate post-approval cycle times (3 to 5 years) and supply chain challenges for global implementation?
   b. How can Industry balance the regulatory requirements for life-cycle management changes between ICH and non-ICH countries?

3. ICH Q12 has the potential to stimulate and promote innovation with regard to continuous manufacturing improvement.
   a. Past initiatives to facilitate post-approval changes have met with limited success. How can stakeholders partner to ensure successful implementation of ICH Q 12 principles this time around?
   b. How can industry develop harmonized approaches for managing life cycle changes in order to create consistency, alignment and efficiency for implementation?

NOTES:
NOTES: