Welcome to the CMC Strategy Forum Europe 2017

The 11th annual CMC Strategy Forum Europe, organized by CASSS, will explore many critical topics focused on improving the quality in development and manufacturing of biopharmaceutical products. A series of plenary sessions and workshops led by experts from global regulatory agencies, academia and industry seek to explore emerging aspects of CMC technology and regulation in areas where existing modalities and systems are undergoing change. Topics will include: Regulatory Update from Around the World; The Continuing Evolution of Product Characterization; Manufacturing Process Development and Control Strategies; Statistical Tools to Evaluate Quality Attributes for Comparability and Biosimilarity; and Opportunities and Obstacles for Accelerated CMC Development. The EBE session will present updates on the following concept papers: A Risk-based Approach to Setting Sterile Filtration Bioburden Limits; A Biopharmaceutical Industry Perspective on the Control of Visible Particles in Biotechnology-derived Injectable Drug Products; and Drug Device Combination Products, as well as the workshop topic: ATMPs – Specific Challenges in Development and Commercialization.

The CMC Strategy Forum is designed to maximize dialog between participants. Presentations are relatively short and focused and set the agenda for the panel discussions to engage all the participants who have experience and expertise to share. It should be important for you to attend this event as we come together to discuss important issues on how to ensure product safety and efficacy for the patients we serve.

We would like to thank the speakers and panel members 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, Bristol-Myers Squibb Company; Eli Lilly and Company; F. Hoffmann-La Roche Ltd.; IPSEN Biopharm Ltd.; MedImmune, A member of the AstraZeneca Group; MSD; Novo Nordisk A/S and Pfizer, Inc. We are grateful for the expert management from CASSS and the audio-visual expertise of Michael Johnston from MJ Audio-Visual Productions. Their experience and guidance in the preparation of this Forum has been invaluable.
ACKNOWLEDGEMENTS

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Monday, 22 May 2017

European Biopharmaceutical Enterprises (EBE) Satellite Session

06:30 – 08:30  Breakfast in the Garden Room Restaurant
(Breakfast is included in the CMC Strategy Forum group sleeping room rate; other attendees / guests can pay individually for breakfast if they are not included in the group room rate)

07:30 – 12:00  Registration in the Muckross Suite Foyer

08:30 – 08:45  Welcome and Introduction to the European Biopharmaceutical Enterprises (EBE) Ongoing Activities and Initiatives in the Muckross Suite
Markus Goese, F. Hoffmann-La Roche Ltd.

Concept Paper 2017 Update: New Initiatives
In the Muckross Suite
Session Chairs: Ronald Imhoff, Janssen Biologics BV and Fionnuala O’Driscoll, Eli Lilly S.A. Irish Branch

08:45 – 09:00  Risk-based Approaches regarding Bioburden Sampling and Limits on ID Sampling of Biologics API
Karoline Bechtold Peters, Novartis Pharmaceuticals Corporation, Switzerland

09:00 – 09:15  A Biopharmaceutical Industry Perspective on the Control of Visible Particles in Biotechnology-derived Injectable Drug Products
Tapan Das, Bristol-Myers Squibb Company, USA

09:15 – 09:30  An Industry Perspective on the Marketing Application Technical Requirements and Regulatory Review Process for Medicinal Product Containing a Drug Delivery Device Component
Serge Mathonet, Sanofi R&D, France

09:30 – 10:00  Panel Discussion – Questions and Answers

10:00 – 10:30  Networking Break in the Muckross Suite Foyer
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<td>10:30 – 10:45</td>
<td>EU Regulatory Activities for ATMPs</td>
<td>Ilona Reischl, AGES-Austrian Agency for Health and Food Safety, Austria</td>
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<tr>
<td>10:45 – 11:00</td>
<td>Critical Quality Attributes for C&amp;GT Products – Enabling Comparability Assessments through Product Development</td>
<td>Ben Thompson, GlaxoSmithKline, United Kingdom</td>
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<tr>
<td>11:00 – 11:15</td>
<td>The Imlygic® Story: A Winding Road to Innovation</td>
<td>Michael Abernathy, Amgen Inc., USA</td>
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<tr>
<td>11:30 – 12:00</td>
<td>Panel Discussion – Questions and Answers</td>
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<tr>
<td>12:00 – 12:15</td>
<td>Concluding Remarks</td>
<td>Barbara Freischem, European Biopharmaceutical Enterprises (EBE), Belgium</td>
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## Monday, 22 May continued…

### CMC Strategy Forum Europe 2017
**Scientific Program Summary**

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<td>13:15 – 17:00</td>
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<td>14:00 – 14:15</td>
<td><strong>CASSS Welcome and Introductory Comments</strong> in the Muckross Suite</td>
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<tr>
<td></td>
<td>Nadine Ritter, <em>Global Biotech Experts LLC</em></td>
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<td></td>
<td><strong>Introduction / Welcome to the 11th European CMC Strategy Forum</strong></td>
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<td>Alistair Kippen, <em>IPSEN Biopharm Ltd.</em></td>
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**Regulatory Updates from Around the World**

*Plenary Session* in the Muckross Suite


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<td>14:15 – 14:45</td>
<td><strong>Biopharmaceuticals – A Regulatory Perspective</strong></td>
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<td>Maeve Lally, <em>Health Products Regulatory Authority (HPRA), Ireland</em></td>
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<tr>
<td>14:45 – 15:15</td>
<td><strong>EU Update on Regulatory Developments</strong></td>
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<td>Pascal Venneugues, <em>European Medicines Agency (EMA), United Kingdom</em></td>
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<td>15:15 – 15:45</td>
<td><strong>US FDA Update: Recent Trends in the Regulation of Biopharmaceuticals</strong></td>
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<td>Chana Fuchs, <em>CDER, FDA, USA</em></td>
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<td>15:45 – 16:15</td>
<td><strong>Networking Break</strong> in the Muckross Suite Foyer</td>
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<tr>
<td>16:15 – 16:45</td>
<td><strong>Regulation of Biological Products in Ghana and the Economic Community of West African States (ECOWAS) Region</strong></td>
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<td>Eric Karikari-Boateng, <em>Food and Drugs Authority, Ghana</em></td>
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<tr>
<td>16:45 – 18:00</td>
<td><strong>Panel Discussion – Questions and Answers</strong></td>
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<td>Chana Fuchs, <em>CDER, FDA, USA</em></td>
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<td>Pascal Venneugues, <em>European Medicines Agency (EMA), United Kingdom</em></td>
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18:00 – 19:00  Welcome Reception in the Malton Gardens

19:00  Adjourn Day One
Tuesday, 23 May 2017

06:30 – 08:45  Breakfast in the Garden Room Restaurant
(Breakfast is included in the CMC Strategy Forum group sleeping room rate; other attendees / guests can pay individually for breakfast if they are not included in the group room rate)

08:00 – 17:00  Registration in the Muckross Suite Foyer

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<th>Time</th>
<th>Event Description</th>
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<tr>
<td>09:00 – 09:10</td>
<td>Introduction</td>
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<tr>
<td>09:15 – 09:40</td>
<td>Technical Innovations – Impact on Regulatory Expectations for Product Characterization</td>
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<td></td>
<td>Steffen Gross, <em>Paul-Ehrlich-Institut, Germany</em></td>
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<tr>
<td>09:40 – 10:05</td>
<td>Analytical Control Strategy for Co-formulated Biologics</td>
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<td>Amit Katiyar, <em>Bristol-Myers Squibb Company, USA</em></td>
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<tr>
<td>10:05 – 10:30</td>
<td>Analytical Characterization of Biologic-Biologic Combinations</td>
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<td>Methal Albarghouthi, <em>MedImmune, A member of the AstraZeneca Group, USA</em></td>
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<tr>
<td>10:30 – 11:00</td>
<td>Networking Break in the Muckross Suite Foyer</td>
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<td>Emmanuelle Charton, <em>EDQM, Council of Europe, France</em></td>
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<td>Amit Katiyar, <em>Bristol-Myers Squibb Company, USA</em></td>
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<tr>
<td>12:00 – 13:30</td>
<td>Buffet Lunch in the Garden Room Restaurant</td>
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**Manufacturing Process Development and Control Strategies**

**Workshop Session Two** in the Muckross Suite

**Session Chairs:** Ralf Gleixner, *Merck Serono* and Ronald Imhoff, *Janssen Biologics B.V.*

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<td>13:30 – 13:40</td>
<td><strong>Introduction</strong></td>
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<td>13:40 – 14:05</td>
<td><strong>Approvable Process Control – Scientific Thinking above Creative Marketing</strong>&lt;br&gt;Amanda Shipman, <em>MHRA-Medicines and Healthcare Products Regulatory Agency, United Kingdom</em></td>
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<td>14:05 – 14:30</td>
<td><strong>Use of Quality by Design Principles for Development of an Integrated Control Strategy</strong>&lt;br&gt;Girish Pendse, <em>Eli Lilly and Company, USA</em></td>
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<tr>
<td>14:30 – 14:55</td>
<td><strong>Analytical Control Strategies: From Molecular Understanding to CQAs, Specifications and Lifecycle Management</strong>&lt;br&gt;Garry Takle, <em>Merck, Sharp &amp; Dohme, USA</em></td>
</tr>
<tr>
<td>14:55 – 15:20</td>
<td><strong>Implementation of an Online UV Monitoring System in Tinzaparin Sodium Manufacturing: A Case Study in Approaches to Manufacturing Development and Strategies to Improve Efficiencies with Regulatory</strong>&lt;br&gt;Robert Kelly, <em>LEO Pharma, Ireland</em></td>
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<td>15:20 – 15:50</td>
<td><strong>Networking Break</strong> in the Muckross Suite Foyer</td>
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<td>16:00 – 17:00</td>
<td><strong>Panel Discussion – Questions and Answers</strong></td>
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<td>Chana Fuchs, <em>CDER, FDA, USA</em></td>
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<td>Robert Kelly, <em>LEO Pharma, Ireland</em></td>
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<td>Greg Naugle, <em>Amgen Inc., USA</em></td>
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<td>Garry Takle, <em>Merck, Sharp &amp; Dohme, USA</em></td>
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<tr>
<td>17:00</td>
<td><strong>Adjourn Day Two</strong></td>
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<td>17:45 – 22:00</td>
<td><strong>Networking Reception and Dinner</strong></td>
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<td><em>Muckross Traditional Farms and Jarveys’ Rest</em></td>
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<td>Buses will begin boarding at 17:45.</td>
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<td>Buses will depart at 18:00.</td>
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<td>MAKE SURE YOU ARE ON THAT BUS!</td>
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Wednesday, 24 May 2017

06:30 – 08:45 Breakfast in the Garden Room Restaurant
(Breakfast is included in the CMC Strategy Forum group sleeping room rate; other attendees / guests can pay individually for breakfast if they are not included in the group room rate)

08:30 – 17:00 Registration in the Muckross Suite Foyer

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<th>Statutory Tools to Evaluate Quality Attributes for Comparability and Biosimilarity Workshop Session Three in the Muckross Suite</th>
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<td><strong>Session Chairs:</strong> Niklas Ekman, Finnish Medicines Agency and Martin Schiestl, Sandoz Biopharmaceuticals</td>
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09:00 – 09:10 Introduction

09:15 – 09:40 Statistical Approaches for Comparability Assessment: A Regulatory Statistician’s Views and Reflections
Andreas Brandt, BfArM-Federal Institute for Drugs and Medical Devices, Germany

09:40 – 10:05 Practical Considerations for the Comparative Assessment of Quality Attributes
Thomas Stangler, Sandoz Biopharmaceuticals, Austria

10:05 – 10:30 What is Comparability? An Updated Perspective
R. Martijn van der Plas, CBG-MEB, Netherlands

10:30 – 10:55 Applying Scientific Considerations and Statistical Approaches in Analytical Similarity Assessment
Jennifer Liu, Amgen Inc., USA

11:00 – 11:30 Networking Break in the Forum Foyer, Level 1

11:30 – 12:30 Panel Discussion – Questions and Answers
Andreas Brandt, BfArM, Germany
Beverly Ingram, Pfizer Ireland Pharmaceuticals, Ireland
Jennifer Liu, Amgen Inc., USA
Thomas Stangler, Sandoz Biopharmaceuticals, Austria
Peter Stjärnkvist, Medical Products Agency (MPA), Sweden
Martijn van der Plas, CBG-MEB, Netherlands

12:30 – 14:00 Buffet Lunch in the Garden Room Restaurant
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<td><strong>Introduction</strong></td>
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</table>
| 14:15 – 14:40 | **Opportunities for Accelerated Cell Line Development and Beyond**  
Christopher Frye, *Eli Lilly and Company, USA* |
| 14:40 – 15:05 | **Risk-based Speed: Approaches for Fast to FIH and Right First Time Commercialization**  
Rachel Dinges, *Bristol-Myers Squibb Company, USA* |
| 15:05 – 15:30 | **Registration Enabling Campaign for Accelerated Development: A PPQ Strategy with Minimal Early Investments to Enable Fast to Market Development for a Promising Monoclonal Antibody**  
John Eschelbach, *Genentech, a Member of the Roche Group, USA* |
| 15:30 – 15:55 | **A Holistic Regulatory Approach to Accelerated CMC Development**  
Seán Barry, *Health Products Regulatory Authority (HPRA), Ireland* |
| 16:00 – 16:30 | **Networking Break** in the Muckross Suite Foyer                     |
| 16:30 – 17:30 | **Panel Discussion – Questions and Answers**  
Seán Barry, *Health Products Regulatory Authority (HPRA), Ireland*  
Brigitte Brake, *BfArM-Federal Institute for Drugs and Medical Devices, Germany*  
Rachel Dinges, *Bristol-Myers Squibb Company, USA*  
John Eschelbach, *Genentech, a Member of the Roche Group, USA*  
Christopher Frye, *Eli Lilly and Company, USA*  
Trent Munro, *Amgen Inc., USA* |
| 17:30 – 17:45 | **Closing Remarks and Invitation to CMC Strategy Forum Europe 2018**  
Kowid Ho, *F. Hoffmann-La Roche Ltd.* |
| 17:45 | **Adjournment**                                                        |
EBE (European Biopharmaceutical Enterprises) of EFPIA has recently again kicked-off several position papers and is working on others. An update will be given on the position papers that have recently been published “A Risk-Based Approach to Setting Sterile Filtration Bioburden Limits” and those that have made some considerable progress such as “Drug Device Combination Products / “A Biopharmaceutical Industry Perspective on the Control of Visible Particles in Biotechnology-Derived Injectable Drug Products”.

NOTES:
Risk-based Approaches regarding Bioburden Sampling and Limits on ID Sampling of Biologics API

Karoline Bechtold Peters

Novartis Pharmaceuticals Corporation, Switzerland

There is no clear origin to the rationale behind the EMA recommended bioburden limit before sterile filtration of not more than (NMT) 10 colony-forming units (CFU)/100 ml (EMA Guidelines of 1996, 2012 and Draft EMA Guideline 2016). The limit has been taken from the pharmacopoeial specification for ‘water for injection to produce bulk’, but lacks scientific basis when applied to final drug products. Instead, a "Risk-based Approach" to bioburden control is proposed, which justifies alternative bioburden specifications that take the product manufacturing process into consideration, in contrast to defaulting to the historical 10 CFU/100 ml limit.

This risk-based approach considers the three main risks at the sterile filtration step of drug product manufacture: (a) variability of the microbiological bioburden method, (b) microbial breakthrough during sterile filtration and (c) microbial by-products and their recovery. In the approach described in this Position Paper, these risks have been assessed for their interaction by means of statistics, and possible risk-mitigating measures and a risk assessment approach for microbial contaminations are described.

EU GMP Annex 8 and CFR21.211.84 are currently being interpreted by some reviewers as well as by some companies that each individual container of an API batch is to be verified for identity before conversion to Drug Product and that satellite samples are not adequate. Here, too, a position paper of the EBE will convey that the high-quality assurance standards in biotechnology justify satellite samples, and that ID sampling of each individual container of biologic API will unacceptably increase the risk of microbial contamination with corresponding risks.

NOTES:
A Biopharmaceutical Industry Perspective on the Control of Visible Particles in Biotechnology-derived Injectable Drug Products

Tapan Das

Bristol-Myers Squibb Company, USA

Occurrence of visible particles in biologic products depends on the manufacturing process, post production handling, attributes of the product formulation, and overall stability of the product. Development of drug product aims to design a robust formulation & process to minimize visible particle formation as well as particle load. All products intended for injection must be visually inspected for various defects including the presence of visible particles as required by the pharmacopeia and cGMP. As a result of the probabilistic nature of detecting particles by visual inspection method, without (zero) visible particles is an unrealistic requirement for QC release/shelf life testing of any parenteral product and especially those of biotechnological origin. This presentation will highlight the key points from a recent position paper prepared by the EBE Biomanufacturing Visible Particle Topic Group (Ref 1) as next steps in influencing the revision of the European Pharmacopoeia monograph on Monoclonal Antibodies for Human Use (2031) and outline emerging topics associated with visible particle control.


NOTES:
An Industry Perspective on the Marketing Application Technical Requirements and Regulatory Review Process for Medicinal Product Containing a Drug Delivery Device Component

Serge Mathonet

Sanofi R&D, France

In the context of the final vote of the European Parliament endorsing the new Regulation on Medical Devices (MDR), the European Medicines Agency has recently initiated a call for comment on a concept paper identifying the need to develop a guideline on quality data requirements for medicinal products incorporating, or used with, medical devices to address instances of inconsistent and incomplete data that are currently being submitted in Module 3 of marketing authorization dossiers, line extension application and variation. The EBE biologics device combination product topic group is currently working on a position paper entitled “An Industry Perspective on the marketing application technical requirements and regulatory review process for medicinal product containing a drug delivery device component with special considerations for integral combination products e.g. pre-filled auto-injectors. The presentation will reflect main Industry comments on EMA concept paper, first consensus reached in the topic group on Module 3 content and location of device information as well as some perspective on the evolving MAA regulatory review process for integral combination products reflecting fruitful exchanges with Notified Bodies.

NOTES:
Panel Members:
Karoline Bechtold Peters, Novartis Pharmaceuticals Corporation, Switzerland
Tapan Das, Bristol-Myers Squibb Company, USA
Serge Mathonet, Sanofi R&D, France

NOTES:
EBE Satellite Session:
ATMP – Specific Challenger in Development and Commercialization Workshop

Session Chairs: Ronald Imhoff, Janssen Biologics BV and Fionnuala O’Driscoll, Eli Lilly S.A. Irish Branch

In past few years we do see a substantial increase of investment worldwide into Regenerative Medicine including Gene and Cell Therapies. New developments comprise for example the retroviral transduction of B-Lymphocytes, the expansion, stimulation or transduction of T cells ex-vivo, the production of individualized tumor vaccines after an analysis of neoepitopes in tumors or Gene-Editing using CRISPR-Cas9 technology. The number of Scientific Advise Procedures of EMA-CAT has increased essentially in the past two years. With the possibility of conditional MAAs, PRIME and Adaptive Pathways EMA has created tools to move these innovative therapies with high potential to address unmet medical needs fast to market. Finally, following Article 5 of Regulation (EC) No 1394/2007 the initiative of the European Commission strives to define own GMP requirements for ATMPs and ATiMPs.

The first presentation by Illona Reischl will shed light on ATMPs from a regulator’s perspective. GSK will describe comparability challenges of ATMP development and commercialization. Amgen will showcase their ATMP platform and the recent Imlygic MA approval in the EU. TiGenix will talk on CMC challenges developing new products (autologous and allogeneic products) from an SME perspective.

NOTES:
EU Regulatory Activities for ATMPs

Ilona Reischl

AGES-Austrian Agency for Health and Food Safety, Austria

High hopes have been placed on Advanced therapy medicinal products (ATMPs) to reshape the treatment of numerous conditions, for which there are currently no or insufficient treatment options. The intrinsic complexity of these products has been widely recognized as has the fact that the regulatory framework might require specific considerations for these types of products. While both developers and regulators are building experience, a number of initiatives are aimed at improving the framework are ongoing. The presentation will provide a brief overview of recent activities

NOTES:
Critical Quality Attributes for C&GT Products – Enabling Comparability Assessments through Product Development

Ben Thompson

GlaxoSmithKline, United Kingdom

Development of cell and gene therapy products for rare diseases with small patient populations provides unique challenges for product development. The value of defining the target product profile and, from that, establishing Critical Quality Attributes early in product development provides utility in managing analytical changes and maintaining comparability of analytical results. Additionally, early establishment of CQAs enables manufacturing process changes and the associated formal in vitro comparability studies. The key learnings and challenges experienced in CMC development of an ex vivo gene therapy product will be reviewed.

NOTES:
The Imlygic® Story: A Winding Road to Innovation

Michael Abernathy

*Amgen Inc., USA*

As we find ourselves in the middle of the biotechnology revolution, the pace with which science is advancing related to genetic and molecular biology is mind-blowing and at times, may appear surreal. Yet, innovation provides hope and solace to patients with severe debilitating diseases where treatment options are limited or often unavailable. Imlygic (talimogene laherpavec) is a small step of hope for patients, specifically those suffering from the later stages of melanoma. As the first oncolytic viral immunotherapy approved in most major markets, and as one of only eight ATMP therapies approved in the EU, Imlygic® provides us with an opportunity to assess how we are managing innovation in this The Age of Biotechnology.

This session will focus on the development of Imlygic® as an oncolytic immunotherapy from its discovery at London College in the UK, to the development of talimogene laherpavec by BioVex Ltd./BioVex Inc., and finally progression of this unique and innovative cancer therapy through commercial production, licensure and launch by Amgen. Challenges presented with this innovative therapy will be discussed related to development, manufacture, testing, safety, storage and handling. We will explore some of the impactful risks associated with the program and discuss several of the concerns related to filing review and inspection as identified by regulatory Health Authorities, in particular EMA, FDA, TGA and Swissmedic.

The session will conclude with a look at the innovative therapies that lie just over the horizon, challenging industry and agency alike to explore transformational opportunities to modernize drug discovery, development, regulations and registration.

**NOTES:**
A Living Medicine: How to Cope with CMC Requirements in the Development of Cell Therapy Products of Autologous and Allogeneic Origin

Pilar Redondo

*TiGenix, Belgium*

Cell therapy products represent an unprecedented complexity in terms of a medicinal product, due to their high structural complexity and the fact that they are a “living” medicine. This generates major challenges in terms of classical CMC approaches regarding process validation and product characterization. This is the case for autologous products where each individual product is made in one manufacturing run. Case examples from two cell therapy products we have developed, ChondroCelect and Cx601, respectively an autologous and allogeneic ATMP, will be presented. These examples will illustrate how CMC requirements can be addressed for e.g. process validation, product characterization, and product release.

**NOTES:**
Panel Members:
Michael Abernathy, Amgen Inc., USA
Pilar Redondo, TiGenix, Belgium
Ilona Reischl, AGES-Austrian Agency for Health and Food Safety, Austria
Ben Thompson, GlaxoSmithKline, United Kingdom

NOTES:
Regulatory Updates from Around the World

Session Chairs: Kowid Ho, F. Hoffmann-La Roche Ltd. and Alistair Kippen, IPSEN Biopharm Ltd.

This session will provide a high level regulatory update from around the world. The trip will start with the latest regulatory updates in the EU and US, before travelling to Economic Community of West African States (ECOWAS), where an overview of regulation of biological products in the region will be presented. The session will end with a panel discussion on pre-planned questions and will address questions from the audience.

NOTES:
Biopharmaceuticals – A Regulatory Perspective

Maeve Lally

Health Products Regulatory Authority (HPRA), Ireland

The biopharmaceutical industry is changing and regulatory agencies are adapting to meet the challenges that are being presented. Most of the large biopharmaceutical countries have a manufacturing presence here in Ireland, producing products from recombinant proteins and monoclonal antibodies through to vaccines and stem cells. New products and technologies are appearing on the regulatory landscape, such as gene therapies, personalised medicines, immunotherapies and others, and regulatory agencies such as HPRA are horizon scanning to ensure that there is a regulatory framework to facilitate these innovations as they move towards authorisation. At HPRA we have established a dedicated Innovation Office for early engagement with stakeholders involved in development of innovative products, devices or technologies. This combined with our Horizon Scanning Group promotes and facilitates increased co-operation and sharing of resources within the organisation. We also support the work of Regulatory Science Ireland as it focuses on biosimilar medicines. My presentation shall focus on some of the challenges which lie ahead as the landscape for biopharmaceuticals changes, and will also provide some examples of lessons that can be learned from CMC/ module 3 dossiers which have recently undergone review.

NOTES:
EU Update on Regulatory Developments

Pascal Venneugues

European Medicines Agency (EMA), United Kingdom

The presentation will provide a regulatory update on the following topics:

- The current state of play on EMA international cooperation, including the recent Mutual Recognition Agreement on GMP between the EU and the US.

- Priority medicines (PRIME) and adaptive pathways, two EMA initiatives to address unmet medical need and timely access;

- Biosimilar medicines.

NOTES:
US FDA Update: Recent Trends in the Regulation of Biopharmaceuticals

Chana Fuchs

CDER, FDA, USA

The success of biopharmaceutical products has led to enhanced interest and investment in the development of these products. Increased knowledge of biopharmaceutical products and their manufacturing processes, the development of new technologies, and communication among manufacturers and regulatory authorities have led to the advancement and increased use of new or improved mechanisms for managing the products throughout their lifecycles. The increased understanding of biopharmaceutical products and processes, combined with advanced analytical techniques and approaches, has also supported the development of biosimilar products and biopharmaceutical “breakthrough therapy” products. A brief introduction and updates to the current FDA perspective of these topics will be presented.

NOTES:
Regulation of Biological Products in Ghana and the Economic Community of West African States (ECOWAS) Region

Eric Karikari-Boateng

Food and Drugs Authority, Ghana

Regulation of Biologics in Africa, especially Sub-Saharan Africa can be said to be in its infantile stage at the moment. Before the publication of the European Medicines Agency (EMA), US Food and Drugs Administration (USFDA) and the World Health Organization (WHO) guidelines for the review of Biosimilar applications, most National Regulatory Authorities (NRAs) in the Sub-Saharan Region of Africa were granting Marketing Authorizations (MAs) to Biosimilar Applications by treating them as biogenerics even though clear and defined regulatory pathways did not exist and also most of these Authorities didn’t have the required competent staff and quality control laboratory capacity to fully evaluate and assure the quality of products they were putting on their respective markets.

With the coming in force of the above-mentioned guidelines, most African NRAs with the help of WHO now have guidelines in place for Biosimilars and other biological products. The United States Pharmacopoeia (USP) Centre for Pharmaceutical Advancement and Training (CEPAT) which is located in Accra, Ghana and the WHO have started building capacity of Regulatory Authorities in the Sub region to review the applications of these biological products in accordance with current best regulatory practices.

Currently, harmonization for the regulation of Biologics including Biosimilar is the key focus of the Africa Union (AU) and is being spearheaded by the African Medicines Harmonization Agency, a department under AU. The harmonization process is being implemented in the various Regional Blocks:

1. East African Community (EAC);
2. South African Development Community (SADC);
3. West African Health Organization (WAHO) a department in the Economic Community of West African States (ECOWAS); and
4. OCEAC (Organization de Coordination pour la lutte contre les Endémies en Afrique Centrale) of central Africa.

This harmonization process is expected to result in the formation of the African Medicines Agency (AMA) in 2018 that would strengthen the technical capacities of member countries through knowledge sharing and ultimately promote public health and standardize the extent of regulation of biological products in Africa whiles reducing the incidence of duplication of functions which will also provide the desired flexibility for sponsors of biological products doing business in Africa.

NOTES:
Panel Members:
Chana Fuchs, CDER, FDA, USA
Eric Karikari-Boateng, Food and Drugs Authority, Ghana
Maeve Lally, Health Products Regulatory Authority (HPRA), Ireland
Patrick Owusu-Danso, Food and Drugs Authority, Ghana
Pascal Venneugues, European Medicines Agency (EMA), United Kingdom

The following questions will guide the panel discussion:

- EU: What is the anticipated impact of the BREXIT on the EU system?
- US: What fundamental changes could occur with the nomination of the new FDA Commissioner?
- ECOWAS: What activities are planned in terms of new guidelines development or implementation of existing ones (e.g. ICH, WHO…)?
- Are EU-US and international mutual recognition agreements providing more effective new drug development strategies?
- How can risk-based approaches expedite early access/adaptive pathways progression towards addressing unmet medical need more effectively within the industry?
- Personalized medicines: challenges and outlook?

NOTES:
The Continuing Evolution of Product Characterization
Workshop Session One

Session Chairs: Brendan Hughes, *Bristol-Myers Squibb Company* and Mark Schenerman, *MedImmune, A member of the AstraZeneca Group*

Product characterization is a key element of product development throughout the lifecycle. This session will address some of the challenges that are encountered with characterization throughout development and includes case studies of how they were resolved. Some of the challenges include characterization of complex biological formulations (e.g., co-formulation of two monoclonals), migrating from pattern similarity to attribute measurement (gels to attribute measurement and criticality assignment), and value and limitations of cell-based potency assays for blocking antibodies (an opportunity for QRM?). This session will include case studies and practical experience from industry sponsors as well as regulatory perspectives in presentations and in the accompanying panel discussions.

**NOTES:**
Technical Innovations – Impact on Regulatory Expectations for Product Characterization

Steffen Gross

*Paul-Ehrlich-Institut, Germany*

Biologics and monoclonal antibodies are routinely used to treat patients. Numerous novel compounds representing new formats are currently in various stages of clinical development. An extended characterization of these molecules is a pre-requisite to guarantee patient safety first and presenting new approaches for the treatment of cancers, infections, inflammatory and autoimmune diseases and other disorders. In addition, innovation in technical development has resulted in more sensitive assays enabling better characterization of the products, e.g. with respect to product-related variants and impurities. The consequences of this progress in assay development for setting up an adequate control strategy will be discussed.

NOTES:
Analytical Control Strategy for Co-formulated Biologics

Amit Katiyar

Bristol-Myers Squibb Company, USA

Co-formulated biologics also known as combination biologics products are being increasingly explored to achieve better clinical outcome as compared to individual agents in complex disease setting. The manufacturing of the co-formulated drug product is achieved by mixing two drug substances in a defined ratio followed by fill and finish. The concept of two drugs in one vial for biologics is gaining more attention due to simpler and effective supply chain logistics. Analytical control strategy is one of the critical aspect to provide high quality drug product to the patients. The challenges for implementation of analytical methods for release and stability methods for co-formulated biologics are dependent on physiochemical properties of individual molecules and ratio of the molecules used for combination product. Here, we discuss the case study of analytical separation methods for co-formulated biologics product for supporting release and stability.

NOTES:
Review of Activity Testing for Pfizer Biologic Molecule

Brian Hassett

Pfizer Ireland Pharmaceuticals, Ireland

Abstract was not available at the time of printing.

NOTES:
Analytical Characterization of Biologic-Biologic Combinations

Methal Albarghouthi

MedImmune, A member of the AstraZeneca Group, USA

Development of biologic-biologic combination drugs is emerging in the biopharmaceutical industry. The combination of biologics present a significant analytical development challenge due to the complexity of the individual components and the limited analytical capability to characterize combinations of proteins. A case study will be presented for a co-formulation of monoclonal antibodies being evaluated as a combination drug. The antibodies have similar structures and physicochemical properties. Limitations of analytical methods and characterization studies employed for single product analysis will be discussed. To address these limitations, new analytical methods were developed to monitor quality. Furthermore, an extensive characterization strategy was developed to compare the critical quality attributes in the co-formulation to the individual products and to assess molecular interactions. The studies concluded that co-formulation product has the same critical quality attributes as the individual components.

NOTES:
Panel Members:
Methal Albarghouthi, *MedImmune, A member of the AstraZeneca Group, USA*
Emmanuelle Charton, *EDQM, Council of Europe, France*
Steffen Gross, *Paul-Ehrlich-Institut, Germany*
Brian Hassett, *Pfizer Ireland Pharmaceuticals, Ireland*
Amit Katiyar, *Bristol-Myers Squibb Company, USA*

The following questions will guide the discussion:

- How close are we to fully-characterizing the patterns seen on modern separation methods and how does this affect specification-setting? Where’s the cut-off in terms of abundance for assigning function for low abundance species?

- What approach are companies taking for setting specifications for release and shelf-life for combinations of protein drugs in the same vial?

- Are companies able to argue for substitution of cell-based bioassays with immunoassays where the mode of action is based on blocking of protein-protein interactions?

NOTES:
Manufacturing Process Development and Control Strategies
Workshop Session Two

Session Chairs: Ralf Gleixner, *Merck Serono* and Ronald Imhoff, *Janssen Biologics B.V.*

The goal of manufacturing process development is to establish a commercial manufacturing process capable of consistently producing drug substance of the intended quality. The intended quality of the drug substance is generally determined through consideration of its use in the drug product as well as from knowledge and understanding of its physical, chemical, biological, and microbiological properties or characteristics, which can influence the development of the drug product.

Guideline ICH Q11 and Q8 have introduced new approaches in manufacturing process development and determination of the Control Strategy, in particular the concept of a design space, however, the Quality Target Product Profile (QTPP), Critical Quality Attributes (CQAs) and linkage to Critical Process Parameters (CPP) and ultimately the determination of an overall Control Strategy (CS) are generally considered minimal deliverables from manufacturing process development.

The current session provides ICH Q 8/11-related implementation examples of manufacturing process development and lessons learned from products recently approved.

- Approaches to manufacturing development and control strategy including strategies to improve control/efficiencies in development with regulatory
- Expansion of the design space concept to Life Cycle Management, in particular the ICH Q12 concept on Established conditions

NOTES:
Approvable Process Control – Scientific Thinking above Creative Marketing

Amanda Shipman

MHRA-Medicines and Healthcare Products Regulatory Agency, United Kingdom

Regardless of the route used to develop a manufacturing process and its controls, for successful marketing authorisation application the proposed process and controls must be able to consistently generate product with quality attributes defined to have clinically proven positive benefit/risk. Scientific thinking is essential for acquiring, interpreting and presenting the data to gain approval and to maintain market supply.

NOTES:
Use of Quality by Design Principles for Development of an Integrated Control Strategy

Girish Pendse

_Eli Lilly and Company, USA_

A systematic approach was developed using QbD (Quality by Design) principles to study and characterize monoclonal antibody production processes. This approach comprises of risk assessment of upstream and downstream process parameters, small scale model development and qualification, process characterization as well as the determination of CPPs (Critical Process Parameters) and PARs (Proven Acceptable Ranges). Executed studies improved process understanding, explored multivariate interactions, and established the relationships between CPPs and CQAs (Critical Quality Attributes). The outcome of the studies was used to develop the integrated control strategy for supporting GMP manufacturing. This approach has been successfully implemented on multiple late stage pipeline molecules including a couple of recently approved monoclonal antibody products. In this presentation, experimental designs and relevant statistical analysis methods will be presented using case studies.

NOTES:
Analytical Control Strategies: From Molecular Understanding to CQAs, Specifications and Lifecycle Management

Garry Takle

Merck, Sharp & Dohme, USA

A robust analytical control strategy is key to ensuring data of the required quality will be produced consistently to support an overall product control program. This presentation will focus on describing how a fundamental understanding of the physicochemical and biochemical structure of a therapeutic molecule leads to the robust identification of critical quality attributes, appropriate testing strategies and the establishment of appropriate specifications. The management and control of analytical robustness over the lifecycle of the product will also be discussed with reference to a monoclonal antibody and a recombinant vaccine example.

NOTES:
Implementation of an Online UV Monitoring System in Tinzaparin Sodium Manufacturing: A Case Study in Approaches to Manufacturing Development and Strategies to Improve Efficiencies with Regulatory

Robert Kelly

LEO Pharma, Ireland

Tinzaparin Sodium is the API used in the Drug Product innohep™ used in the treatment of blood clots (Thrombosis). Tinzaparin Sodium is a Low-molecular Weight Heparin manufactured from the depolymerisation of Heparin sodium which is a polydisperse polysaccaride molecule of biological origin (Porcine mucosa). The manufacture of Tinzaparin Sodium from Heparin Sodium utilises the formation of an unsaturated iduronic acid derivative during the depolymerisation which absorbs ultraviolet light at 235 nm. The change in absorbance (ΔA) is currently monitored using offline sampling. The challenges from implementation of realtime Online UV monitoring (PAT Technoclogy) from a manufacturing development and regulatory perspective are discussed and the strategies used to overcome these challenges.

NOTES:
Manufacturing Process Development and Control Strategies
Panel Discussion – Questions and Answers

Panel Members:
Chana Fuchs, CDER, FDA, USA
Robert Kelly, LEO Pharma, Ireland
Greg Naugle, Amgen Inc., USA
Girish Pendse, Eli Lilly and Company, USA
Amanda Shipman, MHRA-Medicines and Healthcare Products Regulatory Agency, United Kingdom
Garry Takle, Merck, Sharp & Dohme, USA

The following questions will guide the discussion:

- How have companies adapted their development approaches as a consequence of the principles outlined in ICH Q8/11?
- Has the promise of development of a design space materialized and are companies developing and / or submitting it?
- To what extent have companies implemented Quality by Design without claiming a Design Space?
- Recent submissions include at least CQAs, CPPs and Control Strategies – have agency reviewers changed their views on the expected controls in the release and shelf life specifications?

NOTES:
Proper use of statistical tools could facilitate data evaluation and decision making, especially in complex situations where intuition fails. The use of statistics beyond simple descriptive data plots is becoming more common in many areas within CMC. This workshop will focus on the use of statistical tools in setting meaningful limits for manufacturing controls, and for comparing quality attributes in the evaluation of manufacturing changes and biosimilar candidates. This is a contentious field where we aim to increase a common understanding between industry and regulators on the proper use of statistics.

Proper use of statistics requires understanding of the scientific problem to be solved. Therefore, we will not go into details in statistical methodology but focus on the questions to be solved and on the interface between process experts and statisticians.

Case studies from industry and regulators will set the floor for the workshop discussion.

NOTES:
Statistical Approaches for Comparability Assessment: A Regulatory Statistician’s Views and Reflections

Andreas Brandt

BfArM-Federal Institute for Drugs and Medical Devices, Germany

The assessment of analytical similarity of a test and a reference product with regard to quality attributes (QAs) is fundamental for the evaluation of manufacturing changes and biosimilar candidates, requiring a quantitative comparison of test and reference. Statistical methods beyond simple descriptive statistics are increasingly applied for this task. Several approaches based on various statistical concepts have been proposed. Commonly used approaches are variations of methods that derive a reference range based on a sample of reference batches and conclude on similarity based on the coverage of the test batches by this reference range. Alternatively, equivalence testing aiming to show similarity of parameters characterizing the distributions (such as means) has been proposed. However, in the first place, it needs to be decided what constitutes ‘true’ analytical similarity for the QAs of interest, before well-grounded and appropriate statistical methods can be chosen to make fair decisions on similarity based on the limited number of available samples of reference and test product.

An EMA draft 'Reflection paper on statistical methodology for the comparative assessment of quality attributes in drug development' summarizing current regulatory considerations in the EU was recently published for public consultation. Key issues from the reflection paper will be presented. The reflection paper starts from the scratch, discussing that basics such as the unit of observation and whether the sampling strategy results in representative data need to be properly understood before appropriateness of statistical methods can be discussed. Furthermore, the application of a specific statistical method requires considerations on the fulfillment of its underlying assumptions, for example normally distributed data. Additionally, issues regarding commonly used methods are discussed such as limitations of frequently used 'reference range' based methods where concluding similarity is more likely when uncertainty is high. Although the reflection paper describes the framework for an equivalence testing approach, it also clarifies that several conditions need to be fulfilled for a valid application of this approach, including a justification of the equivalence limits. However, the aim of the reflection paper is not to present final solutions but to stipulate the discussion on adequate statistical approaches for similarity assessment among stakeholders.

NOTES:
Practical Considerations for the Comparative Assessment of Quality Attributes

Thomas Stangler

_Sandoz Biopharmaceuticals, Austria_

The analytical comparison of a biosimilar candidate to its reference product generates large amounts of data. With a sufficiently large number of batches of the reference product and biosimilar candidate, the data can be subjected to statistical evaluation. In the recent past, regulators and industry have intensified discussions on the suitability of different statistical approaches and how to integrate the statistical evaluation in the overall assessment of biosimilarity. Regulatory guidelines and reflection papers are under preparation or released for commenting.

This talk presents recent experiences in Sandoz’ biosimilar development projects and regulatory interactions with respect to the use of statistics in the evaluation of biosimilarity. Benefits and limitations of different statistical approaches will be discussed in the context of the scientific evaluation of biosimilarity.

NOTES:
What is Comparability? An Updated Perspective

R. Martijn van der Plas

CBG-MEB, Netherlands

The concept of comparability was developed late 1990s, as a pragmatic way to deal with manufacturing changes. The ICH definition of ‘comparable’ is quite flexible and ICH Q5E underscores that ‘The demonstration of comparability does not necessarily mean that the quality attributes of the pre-change and post-change product are identical, but that they are highly similar and that the existing knowledge is sufficiently predictive to ensure that any differences in quality attributes have no adverse impact upon safety or efficacy of the drug product.’

This pragmatic approach proved highly workable; however, certain fundamental issues were never addressed. This presentation will reflect upon some fundamental issues, e.g. different contexts of comparability; QA assessment and ranking (‘criticality’); low level QAs; ranges versus equivalence of QAs; and the implications of these for statistical approaches.

NOTES:
Applying Scientific Considerations and Statistical Approaches in Analytical Similarity Assessment

Jennifer Liu

Amgen Inc., USA

A biosimilar product is expected to meet the regulatory requirement of being highly similar to its reference product at the time of approval. To demonstrate a biosimilar candidate meets highly similar standards, a well-designed analytical similarity exercise should employ comprehensive and state-of-the-art analytical methods fit for purpose for the intended use, with reliable assay performance, sufficient sensitivity and resolution, and characterized to be meaningful and biologically relevant. The criteria established to assess similarity should be meaningfully derived to provide objective evaluations. Both scientific considerations and statistical approaches are taken to establish similarity assessment criteria which consider reference product profile, analytical method performance, and knowledge for the product quality attribute assessed. Inclusion of appropriate statistical methodologies in the assessment can provide greater confidence and to support similarity conclusions. One of the key challenges for analytical similarity is the assessment of stability-indicating attributes, which could have impact on purity, potency, and safety. We will discuss the design of the similarity study to allow consideration of the profile changes as a function of shelf life, and the statistical approach to assess stability as part of the totality of analytical similarity.

NOTES:
Statistical Tools to Evaluate Quality Attributes for Comparability and Biosimilarity
Panel Discussion – Questions and Answers

Panel Members:
Andreas Brandt, BfArM, Germany
Beverly Ingram, Pfizer Ireland Pharmaceuticals, Ireland
Jennifer Liu, Amgen Inc., USA
Thomas Stangler, Sandoz Biopharmaceuticals, Austria
Peter Stjärnkvist, Medical Products Agency (MPA), Sweden
Martijn van der Plas, CBG-MEB, Netherlands

To following questions will guide the discussion:

• What are the opportunities and pitfalls of statistical tools? What can we expect/not expect from statistical tools?

• Which knowledge/data is required to set meaningful limits for manufacturing controls including release specifications?

• How to set meaningful limits for comparing quality attributes after manufacturing changes and for biosimilar evaluation?

• Is equivalence testing (comparing the mean/average of two populations) a meaningful tool for assessing comparability?

• What are the upsides and downsides of other tools for comparing quality attributes? E.g. descriptive statistics and min-max, tolerance intervals?

• How to foster appropriate use and prevent misuse of statistical methodologies?

• How to best facilitate collaboration between process experts and statisticians?

NOTES:
CMC Development activities for biological products have long lead times and require significant financial investment. Hence they are typically “critical path” items which determine how quickly new (investigational) medicines can reach patients, both in terms of initiation of clinical trials, and commercial availability. Given that an estimated ~80%\(^1\) of investigational medicines entering Phase 1 studies will not be advanced into Phase 3, there is a strong incentive to “fail quickly and fail early”, before financial investments escalate, and to free up capacity in the development pipeline to bring other molecules forward into the clinic. Later in development, it is typically necessary for CMC Development activities for commercial supply to be initiated at risk, ~6-12 months prior to pivotal clinical data read-out. Given a Phase 3 failure rate of ~40%\(^1\), this necessary approach can result in a significant waste of resources.

In this session, presenters from Industry & academia will be invited to identify challenges / obstacles to accelerated development, & present case studies and proposals for how CMC Development lead-times can be reduced and/or taken off the critical path, in a phase-appropriate manner, while continuing to ensure that medicinal products are manufactured to appropriate quality standards. Regulators will be invited to provide their perspectives on the degree of flexibility that may be available at different phases of development, within the boundaries of current regulatory requirements.

NOTES:
Opportunities for Accelerated Cell Line Development and Beyond

Christopher Frye

*Eli Lilly and Company, USA*

Bioprocess development is a technically complex and costly endeavor. Industry often struggles with trying to balance early investment in developing the clinical-enabling manufacturing process against therapeutic candidate attrition rates and the need to ultimately deliver the commercial manufacturing process. Generation of the production cell line is the foundation of bioprocess development and represents a significant part of the overall timeline. In this presentation, approaches will be shared providing potential opportunities for acceleration of cell line development as a focus of the Next Generation Cell Line Development (NGCLD) platform. In addition, risks and benefits of NGCLD will be discussed including enabling new tactical options for reducing bioprocess development timelines.

**NOTES:**
Risk-based Speed: Approaches for Fast to FIH and Right First Time Commercialization

Rachel Dinges

Bristol-Myers Squibb Company, USA

Speed to patient is an important commitment of biopharmaceutical companies. To enable rapid initiation of Phase I studies, we have implemented platform processes, formulations, analytics and specifications, and leverage knowledge and data across products. We have developed a playbook for clone selection and platform assessment, which enables FIH development and ensures speed, while maintaining robust, data-driven decision making. Likewise, our approach to commercial process development includes assessment of technical gaps and risks at all stage gates. As more programs are granted Breakthrough Therapy Designation or Priority Medicines (PRIME) status, we leverage a similar risk-based speed approach to enable rapid commercialization, as well as robust processes and methods for the commercial lifecycle of the product. A few examples will be presented to illustrate our tools and approach.

NOTES:
Clinical development programs are increasingly requiring trials and timelines with extra degrees of flexibility to allow for an accelerated submission based on early positive data. It is becoming more common that a program in Phase I can plan for filing for commercial licensure in less than five years given a certain set of aggressive assumptions. This often places CMC activities on a critical path requiring a large resource commitment at an early stage of clinical development when the likelihood of commercial launch remains unclear.

In this presentation, we explore a case study for a program that has both a low volume demand at launch and limited clinical data, while also having the potential for a fast-to-market strategy gated to positive clinical results. We introduce the concept of a Registration Enabling Campaign (REC) conducted in lieu of a traditional Phase III supply campaign that would provide the Registration Batches for licensure, but also eliminate the need for a traditional PPQ campaign prior to submission or launch. While this approach initially requires an early investment prior to Phase III, it significantly reduces the resources required for a traditional qualification campaign that would be otherwise discarded for a low volume product.

We will present the strategy for the initiation of prospective studies needed to support a Phase III-REC, rationales for study deferrals, and the overall risks associated with analytical quality control systems that must be leveraged at a very early phase in development.

NOTES:
Accelerated development pathways create unique CMC challenges for both industry and regulators. While no one approach can overcome these challenges, several aspects of the Module 3 dossier can be tailored to suit the unique requirements of an accelerated development. These can include use of small scale models, continuous process verification, concurrent validation, Post Approval Change Management Protocols (PACMPs) and the use of Prior Knowledge. The use of small scale models allows applicants to bridge the knowledge gap when relatively few manufacturing runs have been performed by the time of submission. Indeed, regulators now have considerable experience in the evaluation of small scale studies and encourage their use in supporting the process validation scheme. The recent process validation guideline for biotechnology-derived active substances now affords more opportunity to move some aspects of full scale process validation activities to the post approval setting. Moreover, there are now additional opportunities for industry to utilize continuous and concurrent validation activities. The more widespread use of PACMPs allows applicants to secure regulatory endorsement for post approval changes at the time of initial authorisation. This allows for greater certainty in the development plan in the post licensing phase. Stemming from this, I will discuss the advantages and pitfalls of filling with a more “restricted” control strategy which can then be expanded post approval. Finally, much work remains in terms of fully exploiting the promise of Prior Knowledge and the use of platform technology. I will discuss the challenge of how data generated from other products can be used in support of current submissions.
Panel Members:
Seán Barry, Health Products Regulatory Authority (HPRA), Ireland
Brigitte Brake, BfArM-Federal Institute for Drugs and Medical Devices, Germany
Rachel Dinges, Bristol-Myers Squibb Company, USA
John Eschelbach, Genentech, a Member of the Roche Group, USA
Christopher Frye, Eli Lilly and Company, USA
Trent Munro, Amgen Inc., USA

The following questions will guide the discussion:

- If manufacture from a “pool” cell line is confirmed as viable for production of toxicology material, what are the potential opportunities and obstacles to taking the approach one step further, for production of early human clinical study material?

- The PACMP approach in EU has many potential theoretical benefits for scaling up for commercial manufacture in parallel with MAA; however in practice, it is not being routinely employed by Industry. What are the reasons? Is too much specificity required to be practicable? Are less specific PACMPs feasible?

- Concurrent / continuous process verification / validation is well established for some aspects of biotech manufacturing processes (e.g. column resin re-use); what are the opportunities and challenges of extending a CPV approach to other process stages?

- What is prior knowledge? Are there examples where prior knowledge have been successfully used to streamline or accelerate CMC development? How can Industry efficiently and effectively incorporate prior knowledge into the dossier to satisfy regulatory agency needs?

- Industry often needs to engage Regulators early in the development process to obtain buy-in for alternative CMC development strategies. What are the opportunities and challenges for early Regulatory Agency engagement, particularly for investigational products which do not have a “priority” designation (e.g. PRIME, Breakthrough Designation)?

NOTES: