FINAL PROGRAM

CASSS Midwest Discussion Group

Co-chairs:
Michael Boyne, *Biotech Logic*
Khalid Mahmood, *Eli Lilly and Company*

Sheraton Clayton Plaza Hotel
St. Louis, Missouri

October 19-20, 2016
# Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conference Program Partners</td>
<td>3</td>
</tr>
<tr>
<td>Acknowledgements</td>
<td>4</td>
</tr>
<tr>
<td>General Information</td>
<td>5</td>
</tr>
<tr>
<td>Scientific Program Summary</td>
<td>7</td>
</tr>
<tr>
<td>Program and Speaker Abstracts</td>
<td>8</td>
</tr>
<tr>
<td>Career Development Luncheon Roundtable</td>
<td>10</td>
</tr>
<tr>
<td>Roundtable Discussion Point Sheets</td>
<td>11</td>
</tr>
<tr>
<td>Note Paper</td>
<td>20</td>
</tr>
</tbody>
</table>
The Organizing Committee gratefully acknowledges the Conference Program Partners for their generous support of this CASSS Midwest Discussion Group

<table>
<thead>
<tr>
<th>Program Partners</th>
</tr>
</thead>
<tbody>
<tr>
<td>AbbVie, Inc.</td>
</tr>
<tr>
<td>Agilent Technologies</td>
</tr>
<tr>
<td>Cook Pharmica LLC</td>
</tr>
<tr>
<td>Covance, Inc.</td>
</tr>
<tr>
<td>Eli Lilly and Company</td>
</tr>
<tr>
<td>Pfizer, Inc.</td>
</tr>
</tbody>
</table>
Acknowledgements

Special Thanks to all the Program Committee Members who helped develop this Midwest Discussion Group

Program Committee

Sergey Arzhantsev, CDER, FDA
Leslie Bloom, Pfizer, Inc.
Michael Boyne, BioTech Logic
James Carroll, Pfizer, Inc.
Sarah L. Demmon, Eli Lilly and Company
John (J.R.) Dobbins, Eli Lilly and Company
John Dougherty, Eli Lilly and Company
Don Eisenhauer, AbbVie, Inc.
Michelle Frazier, AbbVie, Inc.
Will Hatcher, Cook Pharmica LLC

Julie Heflin, AbbVie, Inc.
Kathy Lee, Eli Lilly and Company
Michelle Lytle, Eli Lilly and Company
Khalid Mahmood, Eli Lilly and Company
Edwin Moore, University of Illinois
Ned Mozier, Pfizer, Inc
Joshua Pecenica, Purdue University
Lesley Redfern, AbbVie, Inc.
Veda Walcott, Cook Pharmica LLC

Roundtable Facilitators

Sally Anliker, Eli Lilly and Company
Kate Bryant, Cook Pharmica LLC
Roland Buhler, Cook Pharmica LLC
Holly Cargill, Pfizer, Inc.
Kimberly Cosky, Covance, Inc.
Olga Friese, Pfizer, Inc.
Julie Heflin, AbbVie, Inc.
Karen Hywood, Eli Lilly and Company
Anupama Jale, AbbVie, Inc.

Katrina Kearns, Pfizer, Inc.
Shelly Kelso, Cook Pharmica LLC
Barbara Rellahan, Amgen Inc.
Ashley Ruth, BioTech Logic
Dawn Ellen Sailer, Eli Lilly and Company
Thomas Schomogy, Pfizer, Inc.
Robert Seevers, Eli Lilly and Company
Amy StCharles, Pfizer, Inc.

Audio Visual

Michael Johnstone, MJ Audio-Visual Productions

CASSS Staff

Stephanie L. Flores, CAE, Executive Director
Julie Fowle, Meeting Coordinator
Anna Lingel, Meeting Coordinator
Linda Mansouria, CMP, CMM, Conference Manager
**General Information**

**Name Badges**
Please wear your CASSS name badge throughout the day.

**Registration**
The registration desk will be open at 8:00 a.m. until 3:15 p.m. on October 20, 2016.

**Welcome Reception**
CASSS will host a welcome reception on Wednesday, October 19, 2016 from 6:00 p.m. until 7:30 p.m. at the Sheraton Plaza Hotel in the Alexander Restaurant. All registered attendees are invited to attend.

**Career Development Luncheon Roundtable**
Successful career progression requires planning. This is particularly the case in the Biopharmaceutical industry where career advancement typically occurs over long time frames. Young scientists may not have a complete understanding of how to plan for a typical career progression, while experienced scientists may be seeking knowledge of how to achieve a mid-career transition. If you are seeking information about career development in Biotech/Biopharma, then please join the CASSS Career Development roundtable session which will be held during lunch. This table topic will be facilitated by Leslie Bloom, *Pfizer, Inc.* and Michelle Frazier, *AbbVie, Inc.* Refer to Page 10 for additional information.

**Roundtable Session**
There are 7 roundtable topics for you to select from. Use this list to determine which discussion you would like to be involved in.

<table>
<thead>
<tr>
<th>Table Topic 1:</th>
<th>Identification of Critical Quality Attributes for Combo Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table Topic 2:</td>
<td>Platform CQA, Study Design or Data, What Approach and Analytical Method</td>
</tr>
<tr>
<td>Table Topic 3:</td>
<td>Forced Degradation to Support QA Assessment</td>
</tr>
<tr>
<td>Table Topic 4:</td>
<td>CQA Established at What Phase, What Approach Use, Stage?</td>
</tr>
<tr>
<td>Table Topic 5:</td>
<td>Risk Assessment – DS and DP, Risk-based Scoring of QA</td>
</tr>
<tr>
<td>Table Topic 6:</td>
<td>How to Develop CQAs for Accelerated Programs</td>
</tr>
<tr>
<td>Table Topic 7:</td>
<td>Use of CQAs in Developing Overall Control Strategies</td>
</tr>
<tr>
<td>Table Topic 8:</td>
<td>Use of CQAs in Developing Overall Control Strategies (Repeated Topic)</td>
</tr>
<tr>
<td>Table Topic 9:</td>
<td>Platform CQA, Study Design or Data, What Approach and Analytical Method (Repeated Topic)</td>
</tr>
</tbody>
</table>
Tables are set with 12 seats to a table. **Table topics are on a first come, first serve basis.** These roundtables will include two facilitators, whose role is to help assist the discussion and ensure a lively exchange, and a scribe, whose role is to make general, anonymous notes about the discussion so others can have a chance to view the discussion even if they could not participate. The discussion notes will be shared with all attendees during the summary period of the program and will be posted to the CASSS program website two weeks after the program is finalized. You will receive notification when the slides are posted.
Scientific Program Summary

THURSDAY, October 20, 2016

08:00 – 15:00  Registration

08:00 – 09:00  Registration and Continental Breakfast in Gallery 1 and 2

09:00 – 09:15  CASSS Welcome and Introductory Comments
Edwin Moore, University of Illinois

09:15 – 09:30  Program Welcome
Khalid Mahmood, Eli Lilly and Company

09:30 – 10:15  A Regulatory Perspective on Assessing Critical Quality Attributes
Patrick Lynch, CDER, FDA

10:15 – 11:00  The Role of the Critical Quality Attribute Assessment in Biotherapeutic Product Development
Catherine A. Srebalus Barnes, Pfizer, Inc.

11:00 – 11:15  AM Break in Gallery 1 and 2 foyer

11:15 – 12:00  Panel Discussion Moderated by: Michael Boyne, Biotech Logic
Panel Members:
Sarah Demmon, Eli Lilly and Company
Martin Gastens, AbbVie, Inc.
Patrick Lynch, CDER, FDA
Catherine A. Srebalus Barnes, Pfizer, Inc.

12:00 – 13:00  Lunch in Gallery 3

13:00 – 13:45  Roundtable Discussions in Gallery 1 and 2

13:45 – 14:15  PM Break and Roundtable Summaries Created in Gallery 1 and 2 foyer

14:15 – 15:00  Summary of Roundtable Discussions by Table Facilitators

15:00 – 15:15  Closing Remarks by Lesley Redfern, Pfizer, Inc.
The fall discussion group will focus on understanding criticality of quality attributes and their role in demonstrating bioprocess control and overall assurance quality. The discussion will include content from other regional, national or international forum organized by CASSS and speakers from industry and regulatory agencies. The program will also provide a platform for networking with both peers and regulatory authorities.

**Program Abstract**

The fall discussion group will focus on understanding criticality of quality attributes and their role in demonstrating bioprocess control and overall assurance quality. The discussion will include content from other regional, national or international forum organized by CASSS and speakers from industry and regulatory agencies. The program will also provide a platform for networking with both peers and regulatory authorities.

**Speaker Abstracts**

**A Regulatory Perspective on Assessing Critical Quality Attributes**  
Patrick Lynch, *CDER, FDA*

This presentation will provide an overview of basic principles for identifying and evaluating critical quality attributes (CQAs) as part of the control strategy for biotechnology products. CQAs are physicochemical, biological, or microbiological attributes that impact product safety, or efficacy, or both. Identifying CQAs for biotechnology products is challenging due to product complexity and heterogeneity. However, an approach based on comprehensive product characterization coupled with risk-based analyses can help focus CQA identification during product development. Once CQAs are identified, understanding their relationship to the manufacturing process can provide a foundation to establish a robust and targeted control strategy. Additionally, as process and product knowledge increase, a refined approach to CQA evaluation can facilitate improvements to the manufacturing process and control strategy. The presentation will address regulatory expectations with regards to CQA development and use of CQAs to inform bioprocessing control strategies.

**The Role of the Critical Quality Attribute Assessment in Biotherapeutic Product Development**  
Catherine A. Srebalus Barnes, *Pfizer, Inc.*

Critical Quality Attributes (CQAs) are defined as “physical, chemical, biological, or microbiological properties or characteristics that should be within an appropriate limit, range, or distribution to ensure the desired product quality” [ICH Q8(R2)]. A robust CQA assessment drives the selection of molecule attributes that are potentially linked to clinical performance and should be monitored as part of process development and product manufacturing to ensure the desired product quality. A thorough understanding of the CQAs for biotherapeutic products is essential to inform the definition of a comprehensive product control strategy (e.g., analytical methods, in-process, release and shelf-life specifications, critical process parameter ranges, etc.). Global health authorities expect that CQAs are controlled within the ranges observed in clinical materials for new product approvals and within the range of clinical or marketed product materials for post-approval changes and biosimilar product approvals. Strong justification and supportive *in vitro* or
in vivo functional studies or clinical studies, may be required to support approval of product specifications for CQAs that exceed clinical or marketed product ranges. The rationale for the CQA assignments and proposed control strategies are core focus areas for global regulatory submissions.

A proposed framework for defining biotherapeutic product CQAs and application of the CQA assignments to define product control strategies will be discussed. Case studies for therapeutic monoclonal antibodies and other recombinant therapeutic protein products will be used to demonstrate the approach. The role of CQAs in the development of biosimilar products will also be discussed. The discussion will include the use of supportive in vitro and in vivo functional testing studies to further elucidate the relationships between specific product attributes and the relevant biological functions to refine CQA assignments.
Career Development Roundtable
Luncheon Discussion

We will have two tables set aside during the lunch period with 10 seats to discuss career development. The facilitators for this table topic are Leslie Bloom, Pfizer, Inc. and Michelle Frazier, AbbVie, Inc. The seating will be on a FIRST COME, FIRST SERVE basis.

Lunch Table Topic

**TOPIC:** Career Development – Transferable Skills

**FACILITATORS:** Michelle Frazier, AbbVie, Inc.
Leslie Bloom, Pfizer, Inc.

**SCOPE:**
We will be discussing career development within the Biotech and Pharma Industries. We will explore myths regarding the numbers of years one has to acquire to attain a desired position of different area or discipline in the industry. We will discuss transferable skills, management experience and strategic skills sets.

**DISCUSSION POINTS:**

1) Is it important to have a degree in the field that you are pursuing?
   a. For example, if the goal is to be a Director of Analytics, does one need a degree in chemistry, biology, etc.? Is a PhD required?
   b. Is this the case for all careers? For example, does this hold true for Regulatory Affairs or Project Management roles?

2) How does one move from technical roles to Regulatory Affairs, Project Management, Quality Assurance, and vice versa?
   a. What are transferable skills in the industry?
   b. How can you gain more cross-functional experience?
   c. How can gain more strategic experience?

3) Is it better to have a more diverse background or focus on one field for many years?
   a. How can one gain more experience in other disciplines while staying in their current position?
**Roundtable Discussion Points**

**TABLE 1**

**TOPIC:** Identification of Critical Quality Attributes for Combo Products

**FACILITATORS:** Barbara Rellahan, *Amgen Inc.*  
Robert Seevers, *Eli Lilly and Company*

**SCRIBE:** Veda K. Walcott, *Cook Pharmica LLC*

**SCOPE:**  
This table will discuss the determination of critical quality attributes for combination products. Combination products present challenges for development of critical quality attributes compared to typical innovator molecules. Table members will provide input based upon their development and regulatory experience with combination products (drug-device or drug-drug). Participants will discuss several key questions in this area.

**BULLET POINTS FOR DISCUSSION:**

1. How are combination product CQAs defined, e.g., are device characteristics considered QAs of a combination product?  
2. What are typical CQAs for combination products?  
3. What questions have you received about CQA determination?  
4. What are your cues to modify or re-evaluate CQAs during development?  
5. How are acceptable ranges for device functionality characteristics identified and justified?  
6. Does validation of device assembly need to be done with validated drug product or can it, like registration stability be done on representative material?
TABLE 2

TOPIC: Platform CQA, Study Design or Data, What Approach and Analytical Methods

FACILITATORS: Kate Bryant, *Cook Pharmica LLC*  
Amy StCharles, *Pfizer, Inc.*

SCRIBE: Ed Moore, *University of Illinois*

SCOPE:
Critical Quality Attributes (CQAs) are the physical chemical, biological, or microbiological properties that determine the product quality. The degree of control of the CQAs should be assessed and prioritized through a rigorous process of determining the risk assessment of the attributes based on product safety and efficacy. Analytical methods used to assess the CQAs are incorporated into the quality control strategy for the manufacturing process. QbD principles may be used to set the analytical range for the methods specific to the manufacturing process. Manufacturing processes used to develop new products that were also used for previously commercialized products are referred to as platform processes. CQAs for the platform process may apply to the new product. However, values for the analytical methods should be assessed for impact on the new product, and modified if the safety and efficacy of the new product are impacted by the platform processes.

BULLET POINTS FOR DISCUSSION:

1. Monoclonal antibodies may use platform processes. Are platform processes used for other biopharmaceutical products, e.g. therapeutic proteins, vaccines, cellular therapies? What specific platform processes are used for these products?
2. What analytical methods are used to assess CQAs for platform processes? How was the analytical range for these methods established?
3. How are CQAs for platform processes applied when a new product is being developed?
4. What data and how much data are needed to support CQAs used for platform processes?
TABLE 3

TOPIC: Forced Degradation to Support QA Assessment of Biotherapeutics

FACILITATORS: Shelly Kelso, *Cook Pharmica LLC*  
Karen Hywood, *Eli Lilly and Company*

SCRIBE: James Carroll, *Pfizer, Inc.*

SCOPE:
This table will discuss forced degradation approaches used to support the assessment of product quality attributes (PQA). Table members will provide examples of best practices for stress studies, characterization of impurities, as well as technical transfer of knowledge and experiences with regulators.

BULLET POINTS FOR DISCUSSION:
1. What is the design of the forced degradation study; what stresses can be used for various degradants; how much stress is the right amount?
2. What type of characterization methods can be used to evaluate the degraded sample/purified degradant?
3. What types of products are formed with various stress conditions?
4. How to leverage degraded samples to support impact to activity/safety and identification of impurities? Are in vitro and/or in vivo studies used?
6. What is the impact to understanding the analytical method capability?
7. How to apply knowledge for process optimization – e.g. light or pH sensitivity may impact product during manufacturing.
8. What regulatory feedback have the participants received regarding PQA?
TABLE 4

TOPIC: At What Phase CQAs Should be Established and What are Some Approaches?

FACILITATORS:  Kim Cosky, Covance, Inc.
               Tom Schomogy, Pfizer, Inc.

SCRIBE: Sarah Demmon, Eli Lilly and Company

SCOPE:
Critical Quality Attributes (CQAs) are the physical chemical, biological, or microbiological properties that determine the product quality. Many companies are using tools to define CQAs. However, there is no specific tool endorsed by regulatory agencies. A phase appropriate approach may be used to define and study CQAs in the process. However, the risk of not gathering sufficient information to justify the control strategy for a CQA that lacks sufficient process knowledge can exist if defined too late in development. Consideration of CQA impact on raw materials and method development will be explored.

BULLET POINTS FOR DISCUSSION:

1. What tool are companies using to define their CQA’s?
2. At what point in the process do potential CQA’s become defined as CQA’s?
3. What is the process for defining pCQA’s?
4. How often are CQA’s evaluated during development?
5. Is it possible for a CQA to drop off the list? If so, what data is needed?
6. Focus of process development – on all CQA’s?
   o Is there a consistent way to define which CQA’s to focus process development?
   o Control points for each CQA’s – in-process controls vs. specs – what is the process used to decide ultimate control strategy
   o Development of upstream and downstream controls to meet criteria – where does the burden lie with controlling an attribute?
7. How do CQA’s fit into raw materials?
   o Are there different risk levels for early addition vs late addition the material into process?
8. Once CQAs are identified, how is the acceptable variability determined in terms of safety/quality expectations, and factoring in process capability?
9. How do CQA’s drive method development – is that phase dependent?
TABLE 5

TOPIC: Risk Assessment – DS and DP, Risk-based Scoring of QAs

FACILITATORS: Dawn Ellen Sailer, *Eli Lilly and Company*
Anupama Jale, *AbbVie, Inc.*

SCRIBE: Don Eisenhauer, *AbbVie, Inc.*

SCOPE:
This roundtable will discuss various approaches for risk-based scoring of Quality Attributes (QAs) when performing process (formulation, analytical) risk assessments. The discussion will focus on the challenges and some examples used during development. How best is the risk assessment updated during development and after process validation?

BULLET POINTS FOR DISCUSSION:

9. Analytical methods in control strategy for detection
10. Should risk scoring be based on patient safety only
11. What criteria used for assigning severity rating?
12. How does one establish scoring system for likelihood of severity occurring?
13. What score(s) represent high, medium, low risk; what score qualifies QA as critical?
14. Case study example with template
### TABLE 6

**TOPIC:** How To Develop CQAs For Accelerated Programs  
**FACILITATORS:** Julie Heflin, *AbbVie, Inc.*  
Holly Cargill, *Pfizer, Inc.*  
**SCRIBE:** Will Hatcher, *Cook Pharmica LLC*

**SCOPE:**
This table will discuss how to develop critical quality attributes (CQAs) for accelerated programs. More and more, companies have programs that need to accelerate to meet unmet medical need, yet the CMC submission package has the same data expectations as a normal development program. Table members will provide areas of challenge and success for clinical trials and marketing applications with a global perspective in mind. Participants will consider the use of unique strategies for defining CQAs for accelerated programs.

**BULLET POINTS FOR DISCUSSION:**
1. How can attribute criticality be developed with minimal data?  
   a. at manufacturing scale  
   b. from the clinical setting
2. How can we leverage platform knowledge from similar/platform programs?  
3. Using QBD approaches (FEMAs, Risk Assessments, etc.) to assess CQAs  
   a. How do you handle an identified CQA after the start of validation batch execution (i.e., post risk assessment analysis)?  
   b. Use of force degradation and other stability studies as alternate approaches in defining CQAs
4. What unique regulatory considerations for CQAs have you encountered for accelerated programs?
TABLE 7

TOPIC: Use of CQAs in Developing Overall Control Strategies

FACILITATORS: Roland Buhler, AbbVie, Inc.
Katrina Kearns, Pfizer, Inc.

SCRIBE: Leslie Bloom, Pfizer, Inc.

SCOPE:
As part of the development process, and eventual preparation for marketing applications, identification of quality attributes and the strategies around control becomes a critical component. Challenges include varied opinions and definitions of attributes and approaches to assure control and obtain agency acceptance while allowing for business opportunities.

BULLET POINTS FOR DISCUSSION:

This round table discussion will focus on these issues through open discussion of current strategies.

1. How do you define non-critical quality attributes vs critical quality attributes and how are those managed in a control strategy?
2. How do you handle control strategy for low occurrence CQAs?
3. What is the role of release testing in your control strategy?
4. Is testing solely focused on confirmation of delivery of the CQAs?
5. Does every CQA require a control point (characterization/process/monitoring)?
6. How do you use internal CQA lists or risk/ranking output in the development of an overall control strategy (control strategy)?
7. Does the use of CQAs in developing an overall control strategy differ across the business (analytical, process, and regulatory for example)?
8. Is there a governance model or review committee for a final control strategy decision?
9. When does your defined control strategy fall in perspective with process validation?
10. Are there particular element(s) of your control strategy that drive delivery/definition of particular CQAs?
**TABLE 8**

**TOPIC:** Use of CQAs in Developing Overall Control Strategies

**FACILITATORS:** Ashley Ruth, *BioTech Logic*  
Olga Friese, *Pfizer, Inc.*

**SCRIBE:** Michelle Frazier, *AbbVie, Inc.*

**SCOPE:**  
As part of the development process, and eventual preparation for marketing applications, identification of quality attributes and the strategies around control becomes a critical component. Challenges include varied opinions and definitions of attributes and approaches to assure control and obtain agency acceptance while allowing for business opportunities.

**BULLET POINTS FOR DISCUSSION:**

This round table discussion will focus on these issues through open discussion of current strategies.

11. How do you define non-critical quality attributes vs critical quality attributes and how are those managed in a control strategy?  
12. How do you handle control strategy for low occurrence CQAs?  
13. What is the role of release testing in your control strategy?  
14. Is testing solely focused on confirmation of delivery of the CQAs?  
15. Does every CQA require a control point (characterization/process/monitoring)?  
16. How do you use internal CQA lists or risk/ranking output in the development of an overall control strategy (control strategy)?  
17. Does the use of CQAs in developing an overall control strategy differ across the business (analytical, process, and regulatory for example)?  
18. Is there a governance model or review committee for a final control strategy decision?  
19. When does your defined control strategy fall in perspective with process validation?  
20. Are there particular element(s) of your control strategy that drive delivery/definition of particular CQAs?
TABLE 9

TOPIC: Platform CQA, Study Design or Data, What Approach and Analytical Methods

FACILITATORS: Sally Anliker, Eli Lilly and Company

SCRIBE: Ned Mozier, Pfizer, Inc.

SCOPE: Critical Quality Attributes (CQAs) are the physical chemical, biological, or microbiological properties that determine the product quality. The degree of control of the CQAs should be assessed and prioritized through a rigorous process of determining the risk assessment of the attributes based on product safety and efficacy. Analytical methods used to assess the CQAs are incorporated into the quality control strategy for the manufacturing process. QbD principles may be used to set the analytical range for the methods specific to the manufacturing process. Manufacturing processes used to develop new products that were also used for previously commercialized products are referred to as platform processes. CQAs for the platform process may apply to the new product. However, values for the analytical methods should be assessed for impact on the new product, and modified if the safety and efficacy of the new product are impacted by the platform processes.

BULLET POINTS FOR DISCUSSION:

1. Monoclonal antibodies may use platform processes. Are platform processes used for other biopharmaceutical products, e.g. therapeutic proteins, vaccines, cellular therapies? What specific platform processes are used for these products?
2. What analytical methods are used to assess CQAs for platform processes? How was the analytical range for these methods established?
3. How are CQAs for platform processes applied when a new product is being developed?
4. What data and how much data are needed to support CQAs used for platform processes?
NOTES:
NOTES: