CMC Strategy Forum North America: 2024

Schedule

Tuesday, 16 July, 2024

07:30-08:30 Washingtonian Foyer

Registration for CMC Strategy Forum North America

Registration will be open until 17:00.

07:30-08:30 Salon C

Rise and Dine: Breakfast

Breakfast will be available until 9:00 AM

08:30-08:45 Salons D - G

CASSS Welcome and Introductory Comments

Joe Kutza

08:45-09:00 Salons D - G

CMC Strategy Forum Welcome and Session Introduction

Marjorie Shapiro

09:00-10:40 Salons D - G

Workshop Session I: The Wide World of Bioconjugates; Stories of Successes and Challenges From Discovery to First in Human Studies

Charles Morgan, Marjorie Shapiro

In this session, the wide range of types of conjugates and conjugate designs, assembly and their clinical uses will be highlighted. The impressive versatility of proteins, peptides, linkers, payloads, and carbohydrates opens many possibilities to explore new product types for many therapeutic, imaging, and prophylactic areas. This session will explore what contributes to success and where challenges arise in the development of protein and peptide conjugates as well as the exchange of ideas and lessons between R&D, CMC, and lifecycle management groups.

Potential questions to be addressed in this session:

What lessons have been learned about product attributes which are relevant to apply to the design and development of new conjugates? For example, to optimize and refine the design to widen the therapeutic index and avoid toxicities or enable dosing flexibility and convenience, which properties of the mAb/carrier and the linker-payload are relevant? At the design phase, how much weight, if any, do assessments of manufacturability, development and CMC factors carry?

Once the development work starts, how do you ensure that the designed molecule can be made consistently, using reliable and cost-effective sources? For production, scale up and supply from Phase 1 to launch, what are the considerations to manage CMO(s), intermediates and product.

Are there methods/tools used for screening in the R&D phase that can then be picked up for development and characterization? What are the considerations for bioassays including their relationship to the mechanism of action?

Session Speakers:

Overview of the Landscape of Bioconjugates: Emerging Applications and Design Considerations
Emily Ross (Holz), *Genentech, a Member of the Roche Group*

Process Development for a Multivalent Conjugate Vaccine
Sarah Sirajuddin, *Merck & Co., Inc.*

An ADC Case Study - A Pragmatic Approach to Innovation
Minh Luu, *Gilead Sciences, Inc.*

Considerations for Developing Oligonucleotide Transport Vehicle Conjugates
Amelia Adams, *Denali Therapeutics*

10:40-11:10 Salon C

Networking Break

Please feel free to stretch, grab coffee, water, and return to the general session room for the panel discussion!

11:10-12:30 Salons D - G

Workshop Session I: Panel Discussion

Charles Morgan, Marjorie Shapiro

Additional Panelists:

Yuefeng Chen, *Eli Lilly and Company*

Claudia Jochheim, *Blaze Bioscience, Inc.*

12:30-13:30 Salons B - C

Networking Lunch

13:30-15:15 Salons D - G

Workshop Session II: Control Strategy and Potency

David Lee, Laurel Savage

In this session we will focus on various aspects of control strategies for bioconjugates and their intermediates. The diversity of payloads, linkers, bioconjugation strategies and biologics to be conjugated, and mechanisms of action necessitates a thoughtful approach to minimize product-related impurities and ensure potency. In this session case studies that cover these issues will be presented.

Session Speakers:

CMC Regulatory Considerations for Antibody-Drug Conjugates and Other Types of Conjugates
Charles Morgan, *Denali Therapeutics*

Antibody Drug Conjugates: Requirements for Characterization and Control of ADCs from a (European) Regulator´s Perspective
Christian Merz, *Paul-Ehrlich-Institut*

Control Strategies for Potency
David James, *Merck & Co., Inc.*

Understanding Impurities in Antibody Conjugates
Jeffery Carroll, *Avidity Biosciences, Inc.*

15:15-15:45 Salon C

Networking Break

Please feel free to stretch, grab coffee, water, and return to the general session room for the panel discussion!

15:45-17:10 Salons D - G

Workshop Session II: Panel Discussion

David Lee, Laurel Savage

Additional Panelists:

Linan Ha, *AstraZeneca*

Pinky Patel, *CDER, FDA*

Nailing Zhang, *CDER, FDA*

17:10-18:10 Salon C

Welcome & Networking Reception

Wednesday, 17 July, 2024

07:30-08:55 Washingtonian Foyer

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07:30-08:55 Salon C

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08:55-09:00 Salons D - G

Welcome Day II & Introduction to Workshop Session III

Dave Bergeson

09:00-10:40 Salons D - G

Workshop Session III: Analytics

Xiaoyu Chen, Carly Daniels

With the ever-growing bioconjugate portfolio, the analytical tools and strategies required to release and characterize these molecules are rapidly evolving to meet the needs of the industry. Antibody-drug conjugates (ADCs) require precise tools in order to ensure product quality and manufacturing consistency. In the conjugate vaccine space, analytical tools are needed to aid in process development, as well as for product characterization and testing. These analytical tools for diverse bioconjugate molecules encompass applications for process-related impurities, product-related impurities, product quality attributes, and product/process understanding via in-depth characterization. The complexity of these bioconjugate molecules present many analytical challenges during development. In this session, we aim to cover how analytical tools have been utilized for process development of conjugate vaccines, characterization and quality control of ADCs, and other analytical challenges faced across the bioconjugate industry.

Session Speakers:

Application of Advanced Analytics to Support Glycoconjugate Vaccine Process Development
Kelly Sackett, Pfizer, Inc.

Honing Analytical Methods for Next Generation ADCs
Chunlei Wang, *AstraZeneca*

Designing Analytical Development and Control Strategies for ADCs Based on Diverse Drug Linker Properties
Chris Leiske, *Pfizer, Inc*.

Investigation of High Molecular Weight Size Variant Formation in Antibody-Drug Conjugates: Microbial Transglutaminase-Mediated Crosslinking
Yimeng Zhao, *Regeneron Pharmaceuticals, Inc.*

10:40-11:10 Salon C

Networking Break

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11:10-12:30 Salons D - G

Workshop Session III: Panel Discussion

Xiaoyu Chen, Carly Daniels

Additional Panelists:

John Cipollo, *CBER, FDA*

Juliana Kretzinger, *Eli Lilly and Company*

Jun Liu, *CDER, FDA*

Dennis Neeld, *Pfizer, Inc.*

12:30-13:30 Salon C

Networking Lunch

13:30-15:15 Salons D - G

Workshop Session IV: Leveraging Learnings From Global Approvals; Case Studies of Post Approval Change Management

Nomalie Jaya, Michelle Lee Lytle

In this session we will focus on case studies from globally approved bioconjugates while touching on lifecycle management and successful incorporation of learning from globally approved bioconjugates to late-phase CMC development. We will hear from regulators and innovators on the following topics among others:

- Post approval comparability including point of comparability assessment and appropriate attribute assessment at the intermediate steps.
- Challenges as an outcome of differences in global change variation classification for intermediates of bioconjugates.
- Considerations for manufacturing facility utilization and change-over.

Potential questions to be addressed in this session:

- What are the risks and benefits to approaching comparability assessment at the point of change vs. throughout the bioconjugate supply chain from intermediates to DS and DP?
  - Is a comparability exercise necessary for the downstream steps or is routine batch analysis data sufficient?
  - Are there examples of successful approaches such as taking a regulatory commitment to provide downstream data?
  - Since added nodes in the supply chain is a complicating element for bioconjugates, are there examples of flexibility in implementing changes globally?
- Are there unique comparability learnings in bioconjugates therapies for clinical (pre-approved) comparability exercises?
- Are we still applying the same quality standards to the intermediates of bioconjugates as the DP? What would it take to apply a subset of appropriate testing to an intermediate compared to DP?
- Based on the HA, there may be differences in the treatment of mAb and DL intermediates leading to differences in global variation classification (substantial change vs. not based on the HA). Are there strategies for harmonizing between HAs?
- With regard to specific facility controls for ADCs, have there been success in mixing modalities within the same suite/same manufacturing facility?
  - Do biologic expectations for facility submission content and inspection readiness apply to the small molecule synthesis?
- How can we apply lessons learned from lifecycle management of marketed therapies to improve CMC development and regulatory submissions?
- Is there a generally accepted methodology for presenting bioconjugates in a dossier? Do all regions accept a similar approach?
- How have Sponsors successfully applied learning from one bioconjugate into new commercial submissions?
- To what degree have we used PMCP and other regulatory tools to facilitate lifecycle improvements?
- What is the global regulatory perspective in utilizing drug master files (DMFs) to submit drug-linker content?

Session Speakers:

The Journey of Enhertu — Four Years of Commercialization
Meng-Jung Chiang, Daiichi-Sankyo Inc.

Regulatory Considerations for Bioconjugates from the Small Molecule Perspective
Kanny Wan, *CDER, FDA*

Patient-Centric Comparability Approaches for Antibody Drug Conjugates

Richard Seipert, *Genetech, a Member of the Roche Group*

Regulatory Considerations for Bioconjugates From a Biologic Perspective
Felix Jules, *Health Canada*

15:15-15:30 Salon C

Networking Break

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15:30-16:50 Salons D - G

Workshop Session IV: Panel Discussion

Nomalie Jaya, Michelle Lee Lytle

Additional Panelists:

Kavita Aiyer, *Pfizer, Inc.*

Minh Luu, *Gilead Sciences, Inc*

16:50-17:00

Closing Remarks and Invitation to CMC Strategy Forum North America 2025