Biologics Stakeholder Forum (SF) charter

The goals of the Biologics Stakeholder Forum are:

1. To learn the needs of biologics stakeholders that may intersect with USP's core capabilities.

2. To share new information with the stakeholders and obtain feedback.

3. To recruit volunteers to support USP's Council of Experts.

4. To identify subject matter experts who can provide guidance or resources to support the execution of USP's biologics strategy.

2021 Biologics SF planning committee

▶ Ed Chess, Chair, Consultant

▶ Manuel Batz (Merck Group, Germany)

▶ Jonathan Bones (NIBRT, Ireland)

▶ Gael Debauve (UCB, Belgium)

▶ Victoria Dohnal (BIO, USA)

▶ Himanshu Gadgil (Enzene Biosciences Ltd., India)

▶ Mike Mulkerrin (ADC Therapeutics, USA)

▶ Linda Narhi (Consultant, USA)

▶ Sonia Pagliusi (DCVMN, Switzerland)
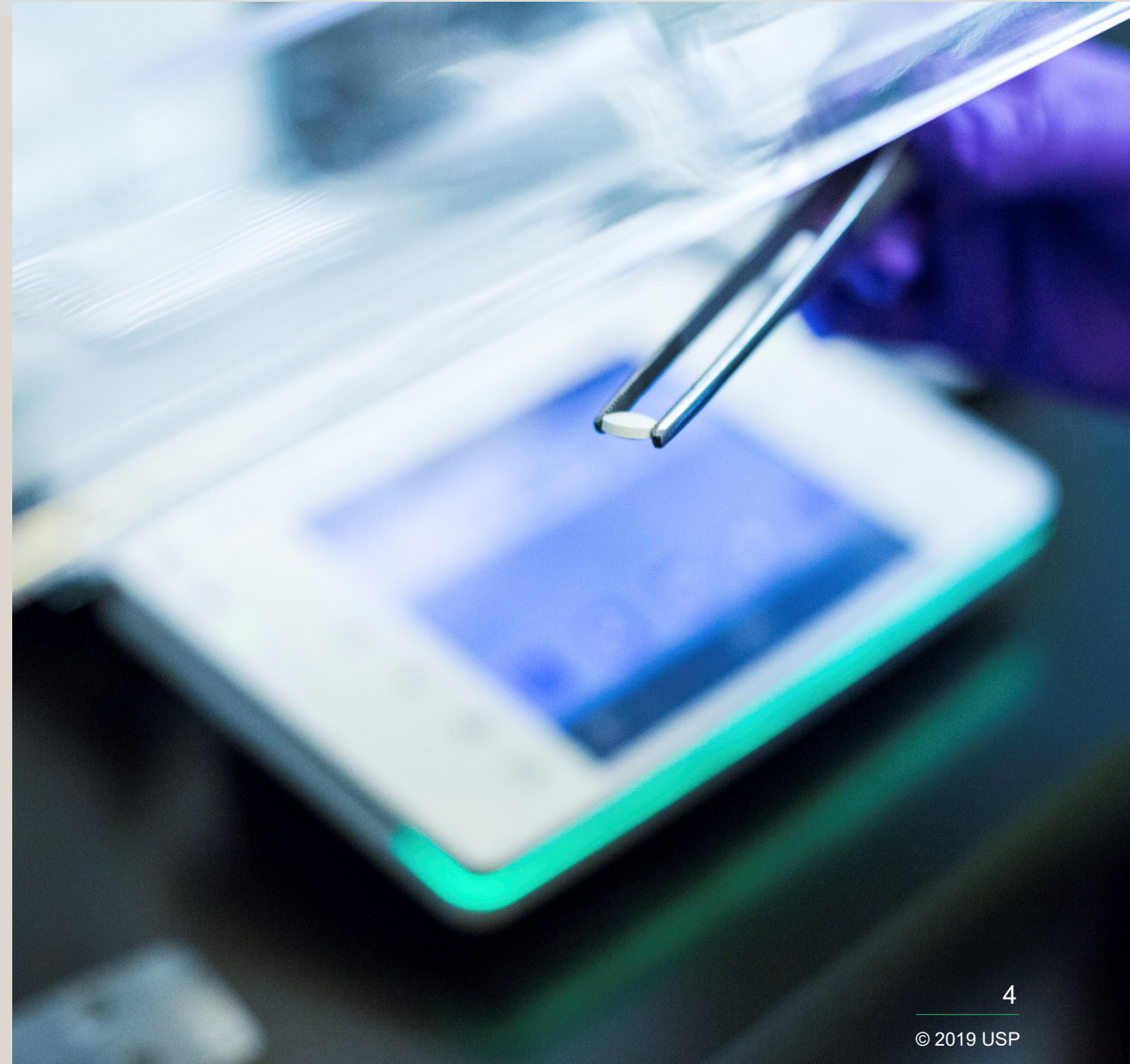
First Biologics SF planning committee members

➢ Edward K. Chess, Chair, Consultant

➢ Wendy Saffell-Clemmer, Vice Chair, Baxter

➢ Matthew Borer, Lilly

➢ James W. Brown, Aldevron

➢ Narendra Chirmule, SymphonyTech

➢ Hillel P. Cohen, Sandoz

➢ Earl Dye, Consultant

➢ Michael Gu, Wuxi

➢ Mo Heidaran, Paraxel

➢ Anne Kroll Kristensen, NovoNordisk

➢ Tina Morris, AAPS

➢ Yeowon Sohn, Consultant

➢ Darin J. Weber, Medeor Therapeutics

Introduction to multi-attribute methods

▸ A multi-attribute method could use any technology that allows a scientist to investigate multiple quality attributes at the same time

   – Peptide-based mass spec has emerged as the most mature and widely used platform for MAM

▸ In 2015, Rogers et al. (Amgen) published the first paper on an LC-MS-based MAM method for monoclonal antibody therapeutics

   – Amgen has implemented MAM in the QC environment, replacing 4 traditional methods: peptide mapping, CE, CEX, and glycan analysis

▸ Benefits of MAM

   – Improved efficiency

   – More detailed assessment of quality attributes

   – Aligns well with QbD concepts

REPORT

mAbs 7:5, 881–890; September/October 2015; © 2015 Amgen Inc.

Development of a quantitative mass spectrometry multi-attribute method for characterization, quality control testing and disposition of biologics

Richard S Rogers[†,*], Nancy S Nightlinger, Brittney Livingston[†], Phil Campbell, Robert Bailey[#], and Alain Balland[§]

Analytical Sciences; Amgen Inc.; Seattle, WA USA
[†]Present affiliation: Just Biotherapeutics; Seattle, WA USA
[#]Present affiliation: Zymeworks; Seattle, WA USA
[§]Present affiliation: Boehringer Ingelheim Pharma GmbH & Co. KG; Biberach an der Riss, Germany

Topics & Speakers

▶ USP Introductions

– Ron Piervencenzi, Ph.D.,USP

– Fouad Atouf, Ph.D., USP

▶ Development and Application of a Multi-Attribute Method (MAM)

– Jette Wypych, Ph.D., Amgen

▶ Enhancing Biotherapeutic Process and Product Knowledge with the Multi-Attribute Method (MAM)

– Andrew Dawdy, Ph.D., Pfizer

▶ Quality Considerations for the Multi-Attribute method (MAM)

– Sarah Rogstad, Ph.D., FDA

▶ USP Standard to Support Multi-Attribute Methods (MAM) and Mass Spectrometry,

– Diane McCarthy, Ph.D., USP
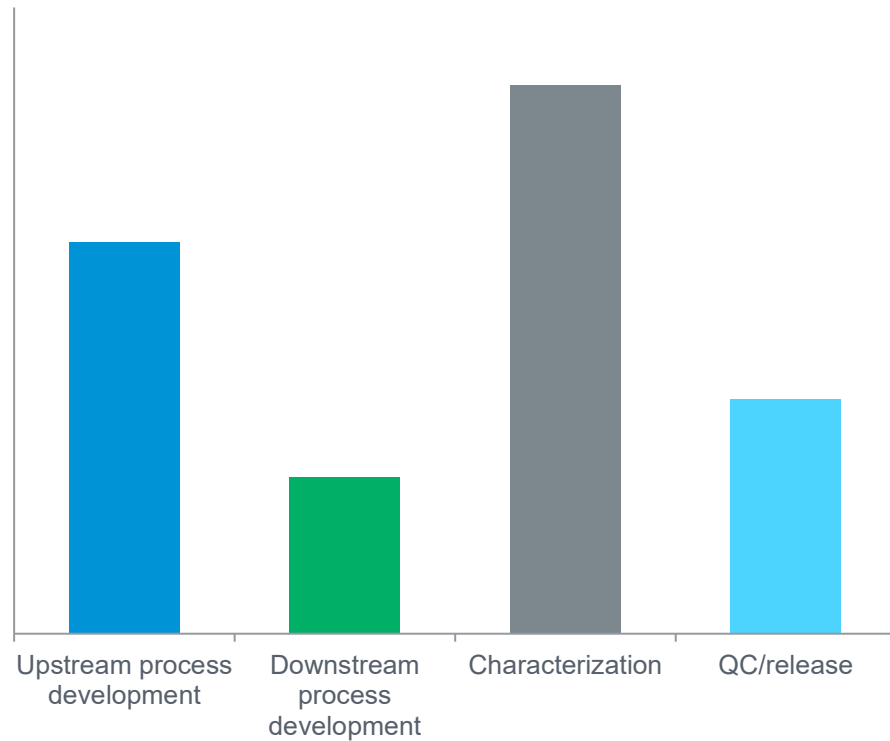
Discussion and Outcomes

▶ Breakout sessions

   – Best practices

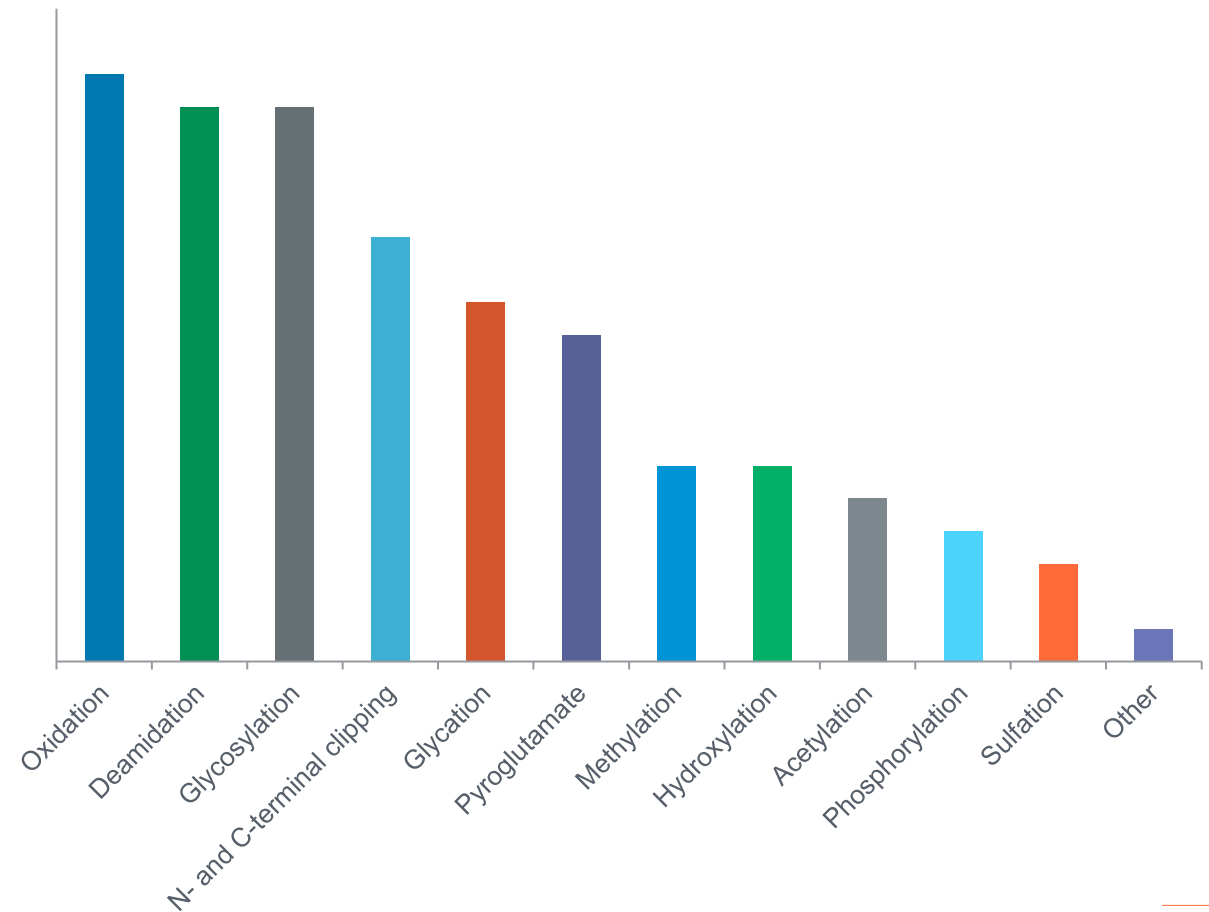   – Opportunities for standards

▶ Recommendations

   – There is a need for best practices for MAM and attendees supported developing a general chapter on best practices for MAM

   – Physical standards will be useful, with particular interest in matched sets of intact and pre-digested mAbs

     • Pre-digested mAb standard was already recommended by the Mass Spec Peptides working group, but forum emphasized need for matched set for each of the USP mAb standards

Survey results

Where in the product lifecycle are you using MAM?

Upstream process development | Downstream process development | Characterization | QC/release

Which PTMs do you typically monitor in MAM/ peptide mapping?

Oxidation | Deamidation | Glycosylation | N- and C-terminal clipping | Glycation | Pyroglutamate | Methylation | Hydroxylation | Acetylation | Phosphorylation | Sulfation | Other

MAM general chapter Expert Panel members

- Edward Chess, Chair, Consultant
- Rachel Chen, Biogen
- Disha Dadke, Aurobindo Biologics
- Andrew Dawdy, Pfizer
- Yuting Huang, Pfizer
- Anita Krishnan, Biocon Biologics
- Zhirui (Jerry) Lian, Eli Lilly and Company
- Benjamin Moore, Genentech
- Yuko Ogata, Just-Evotec Biologics
- Da Ren, Amgen
- Lei Wang, Takeda
- Christopher Yu, Genentech
- Ying Zhou, Teva Pharmaceuticals

MAM general chapter outline

1. Introduction

2. General Description

3. Sample Preparation

   – Strategies to reduce variability and artifacts

   – Manual and automated techniques

4. System Readiness

   – Instrument suitability

   – Criteria for assessing individual spectra

5. Software

   – Critical features and considerations

6. Targeted Analysis

   – Strategy for monitoring known quality attributes

7. New Peak Detection

   – Importance for different applications

   – Best practices for setting thresholds, optimizing performance

8. Product Development

  – Use in product characterization

  – Application to process characterization

9. Qualification and Validation

  – Establishing system suitability

  – Method transfer

10. Production

  – DS vs DP testing

  – Considerations for setting specifications when bridging from traditional method to MAM

  – Lifecycle management

11. Intact and Subunit Workflows

Thank You

Empowering a healthy tomorrow