MAM in streamlined biosimilar development

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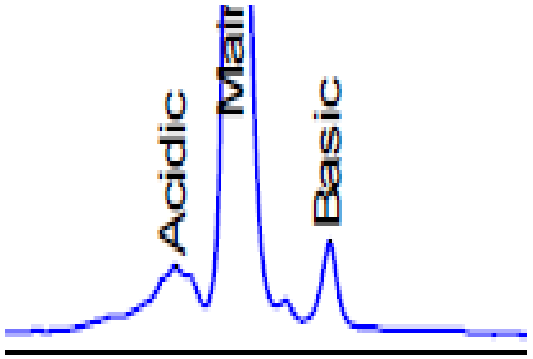
Enabling Affordable Access to Lifesaving Biosimilars, Worldwide

Development considerations of MAM

Conventional methods vis-à-vis MAM

- ✓ Enriched variants (stressed/process intermediates) aid in cross-mapping attributes between both formats
- ✓ Two case studies to discuss key development considerations:
  - ✓ CS 1 – product with cysteine related modifications (NR-MAM)
  - ✓ CS 2 – product with high sialylation (R-MAM)

	Case study 1	Case study 2
cysteinylation	✓	
glutathionylation	✓	
sulfonylation	✓	
DSB scramble	✓	
deamidation	✓	✓
glycation	✓	✓
sialylation	✓	✓
subunit fragments	✓	

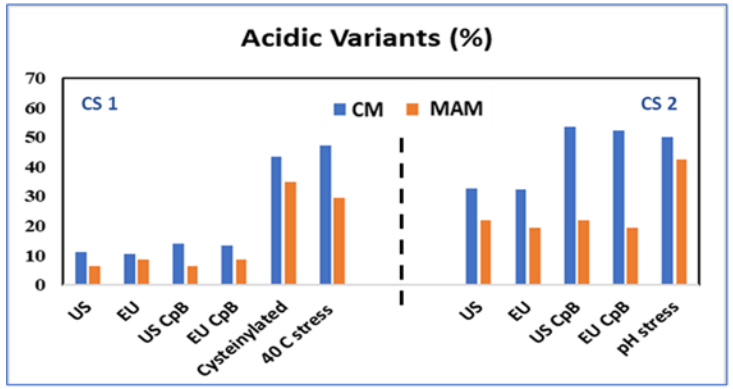


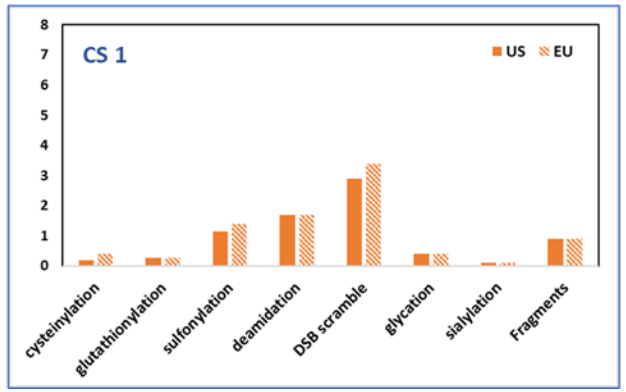
	Case study 1	Case study 2
Pyroglutamate	✓	✓
C-term lysine	✓	✓
Met oxidation	✓	✓
Proline amidation	✓	

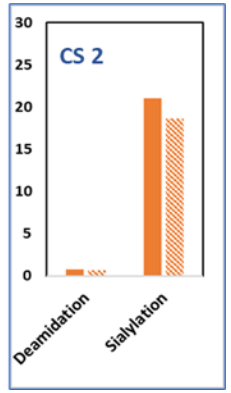
- ✓ Key advantages of MAM
  - differentiates overlapping chromatographic species; enables accurate detection/estimation of PTMs
  - better relationship mapping of product quality attributes with clinical performance
  - better process control of critical quality attributes

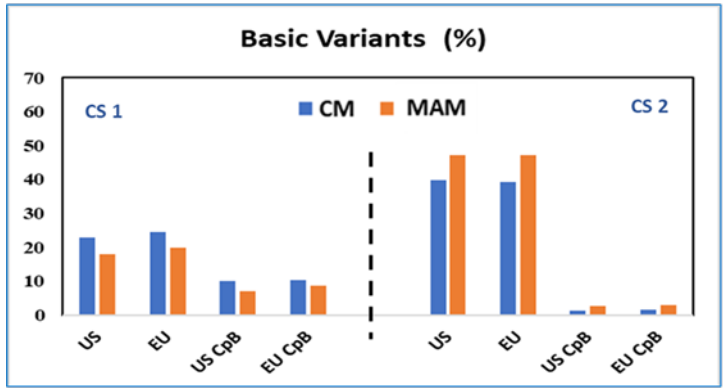
Development considerations of MAM – charge variants

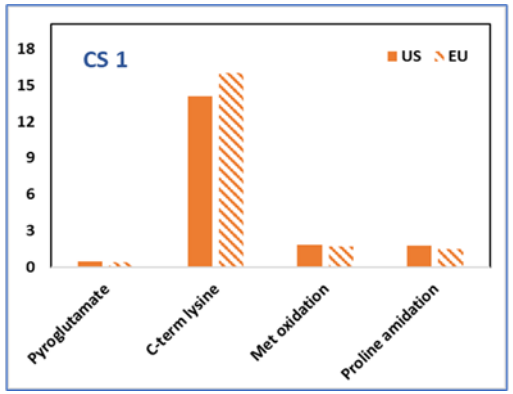
Attribute-wise comparison of CEX Vs MAM with US and EU sourced products (n= 3 to 9)

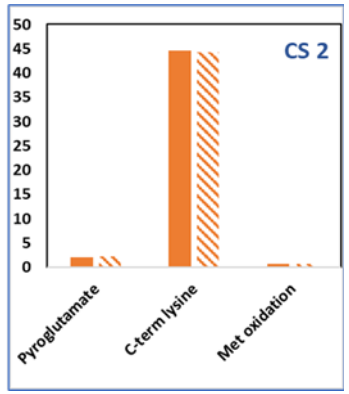








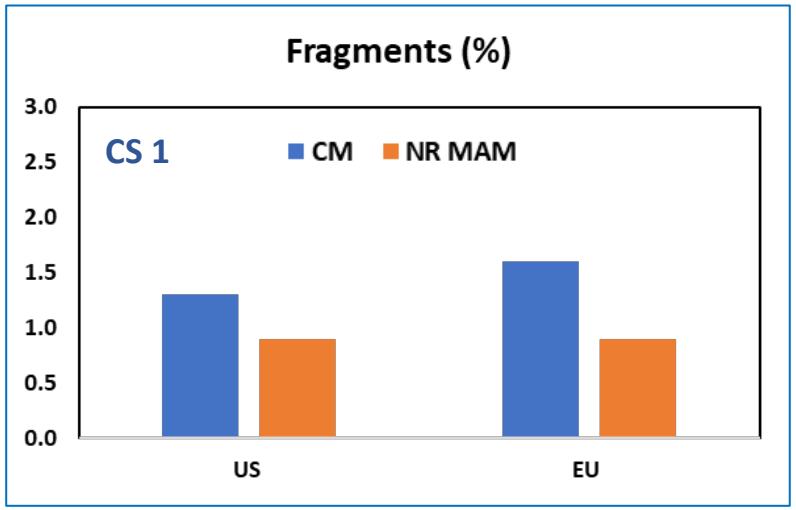


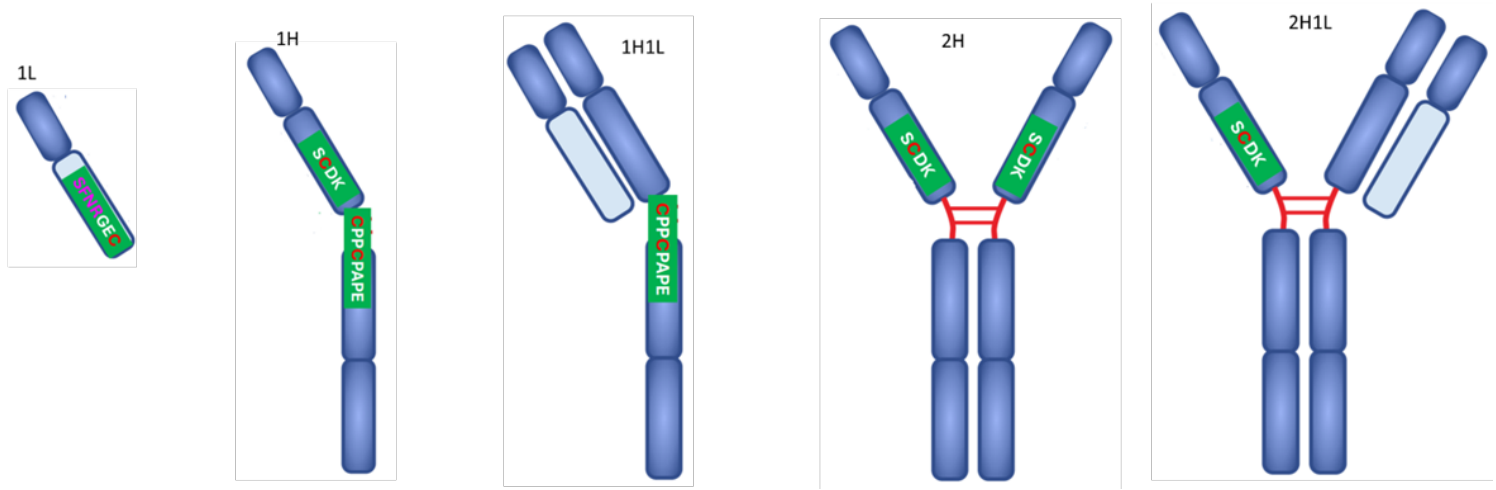


- ✓ **Specific acidic and basic species are overlapping in CEX, but more accurately quantifiable in MAM**
- ✓ **Charge variants elute as per net charge in CEX method and hence PTM estimation is complex**
- ✓ **Products containing a combination of acidic and basic variants need additional treatments like CpB digestion/desialation in CEX**
- ✓ **US and EU origin products are comparable in both CEX and MAM**

Development considerations of MAM – subunit fragments

Attribute-wise comparison of NR-CE-SDS Vs MAM with US and EU sourced products (n=3)



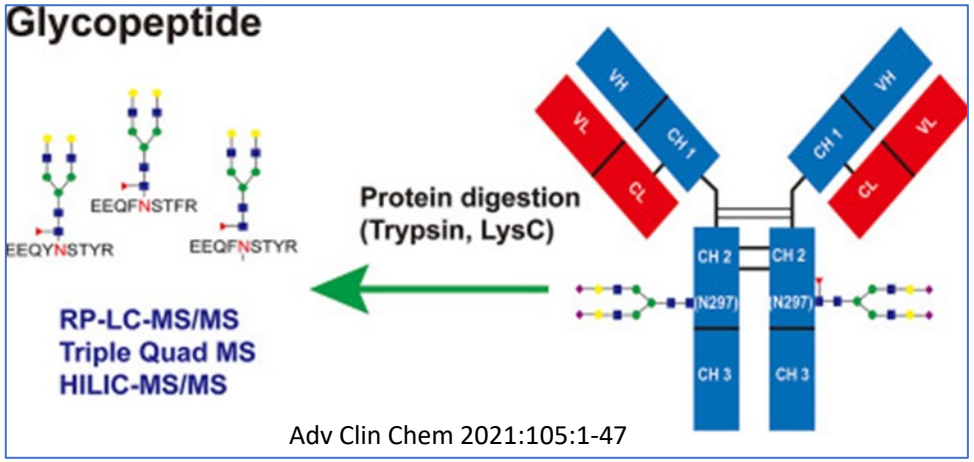


Diagnostic peptides	L	H	HL	HH	2H1L
SFNRGEC* and/or GEC*	✓				
SC*DK		✓		✓	✓
C*PPC*PAPE		✓	✓		

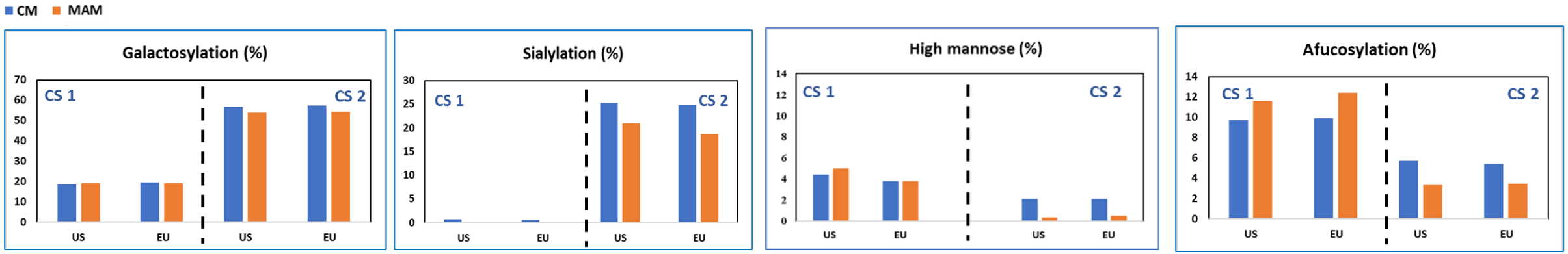
- ✓ Non reduced format of MAM is capable of estimating subunit-based fragments through diagnostic peptides
- ✓ US and EU origin products are comparable in both NR-CE-SDS and MAM

Development considerations of MAM – glycan variants

Attribute-wise comparison of HILIC Vs MAM with US and EU sourced products (n= 3 to 9)

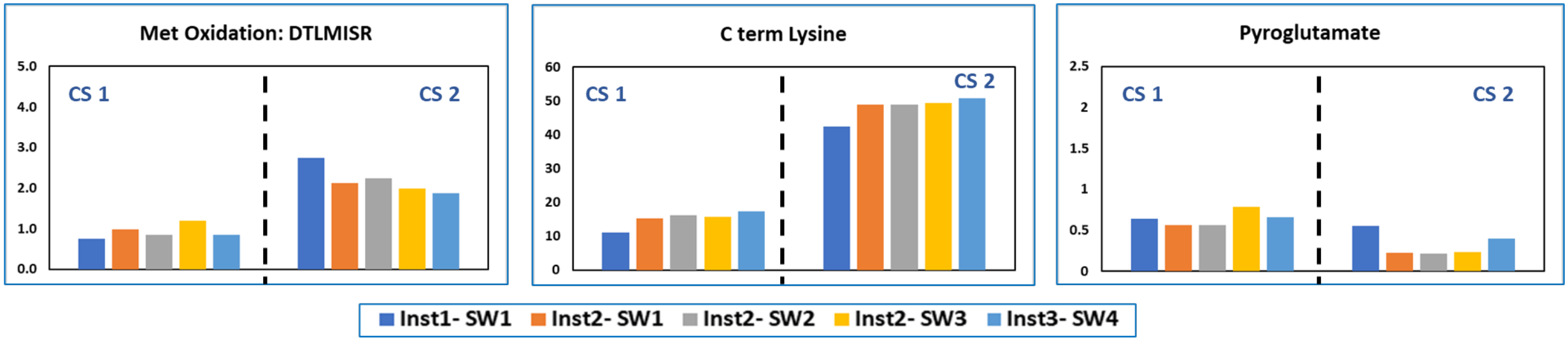


- ✓ **MAM is capable of estimating N-glycans in mAbs through the consensus glycopeptide EEQYNSTYR**
- ✓ **Glycan variants are largely comparable across HILIC and MAM**
- ✓ **US and EU origin products are comparable in both HILIC and MAM**



Scalability considerations of MAM

Portability of MAM - MS platforms



- ✓ **Comparable estimations across instruments and processing software**
  - ✓ **Orbitrap and TOF**
  - ✓ **"HRMS" and "MS only" models**
  - ✓ **Processing software (vendor dependent/independent)**

Conclusion

- ✓ New generation instrumentation supports the implementation of MAM throughout the life-cycle of the product, spanning research and quality control labs
- ✓ Conventional methods provide information about combination of modifications; usefulness of this info needs careful evaluation
- ✓ MAM can potentially replace multiple conventional methods such as CEX/cIEF, HILIC, CE-SDS, Identity methods during DS/DP batch release
- ✓ MAM as a technology is aligned to research priorities of FDA's BsUFA III enabling streamlined biosimilar development

Thank you

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