

## GMP compliant Characterization of Therapeutic Antibodies according to ICH Guidelines Q6B

### Characterization of Therapeutic Antibodies

The complex nature of antibodies as therapeutics presents numerous challenges during development and manufacture. These protein therapeutics are often heterogeneous and therefore complex to characterize. Overall small changes in the protein structure, such as glycosylation, disulfide linkage or presence of some low level impurities (e.g. deamidation/oxidation), can have an important influence on biological activity and efficacy and are therefore important considerations in the regulatory process.

#### Quality Assurance and Regulatory Affairs

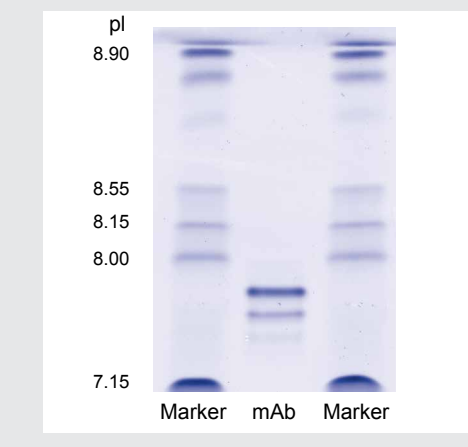
Protagen Protein Services GmbH (PPS) has extensive experience in providing structural analytical services to characterize antibody products and to provide data required by

- ▶ ICH Q6B guidelines,
- ▶ FDA's concept of well characterized biological products,
- ▶ EMA guideline on development, production, characterization and specifications for monoclonal antibodies and related products.

Protagen Protein Services performs comprehensive analytical service packages, as well as individual analyses validated to fulfill the latest regulatory demands and GMP standards.

## Antibody Characterization

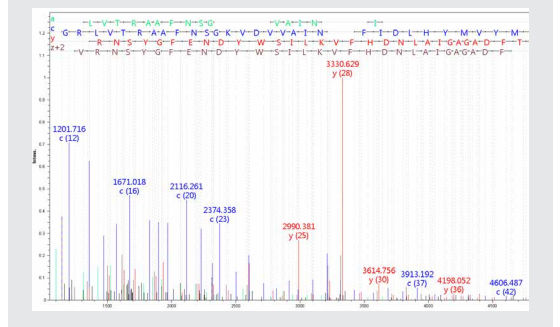
### IEF Zoom



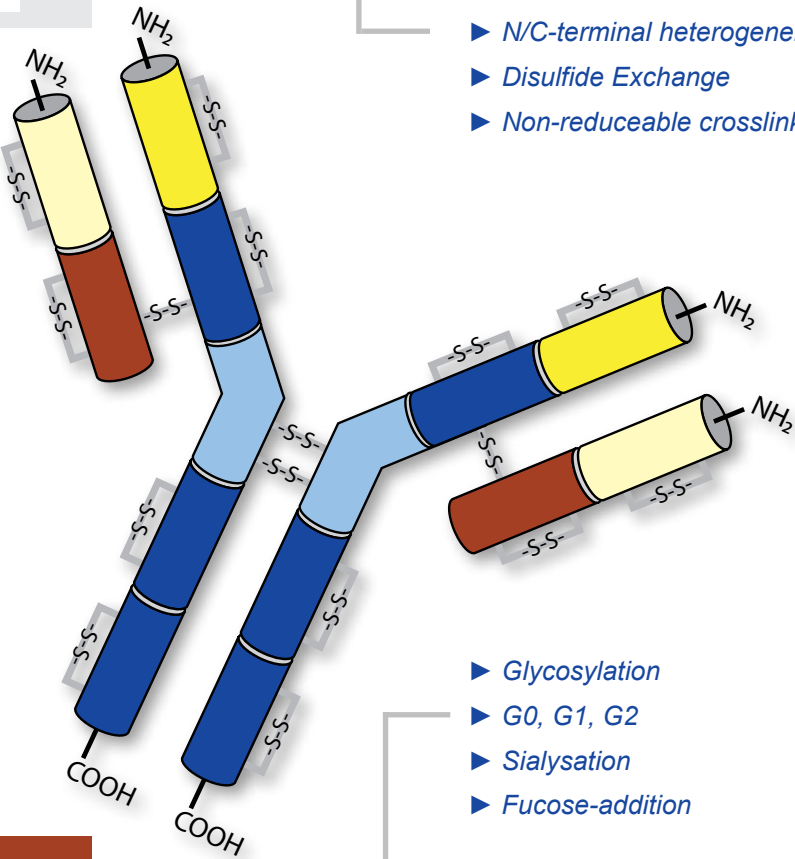
- ▶ Deamidation
- ▶ Oxidation
- ▶ Isomerization
- ▶ Glycation

- ▶ Dimer formation and aggregation
- ▶ Change in AA sequence
- ▶ Change in higher order structure

### MALDI-MSD (In-Source-Decay)



- ▶ N/C-terminal heterogeneity
- ▶ Disulfide Exchange
- ▶ Non-reduceable crosslinking

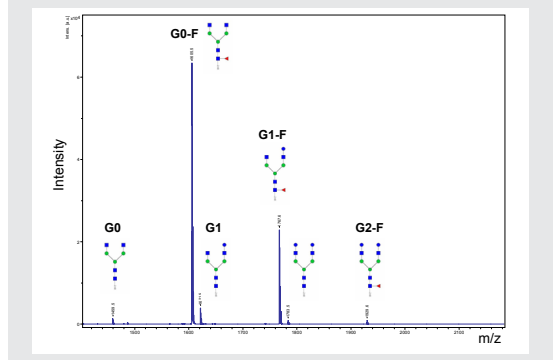


- ▶ Glycosylation
- ▶ G0, G1, G2
- ▶ Sialylation
- ▶ Fucose-addition

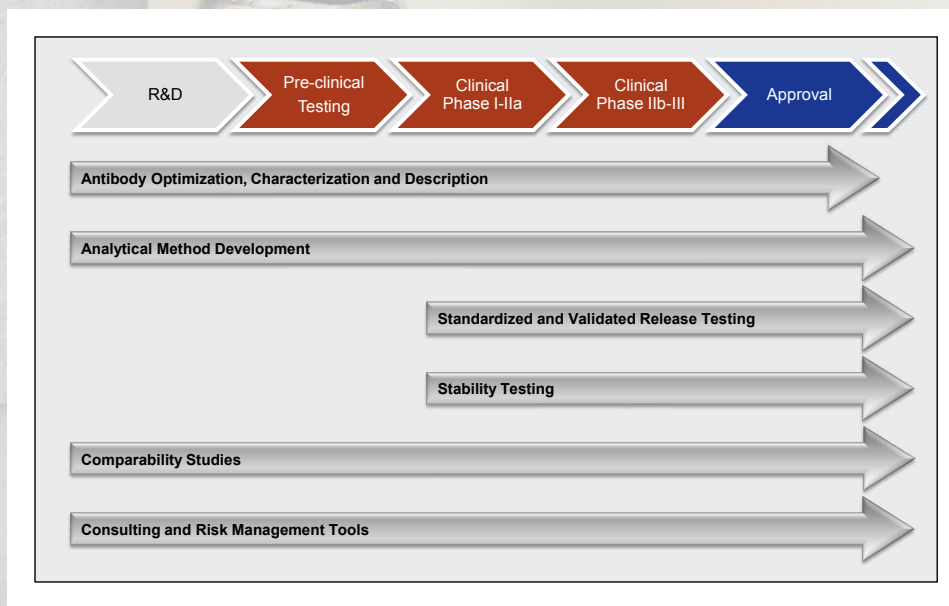
### Full Peptide Mapping



### MALDI Glycan Mapping



### Analytical Services throughout the complete antibody development process



Analytical services of Protagen Protein Services cover the full scope of the antibody development process, from early R&D to final approval.

Protagen Protein Services offers its clients a one-stop shop for all protein analytical and regulatory requirements.

### Example for an Antibody Comparability Study

#### Goal

The goal was to assess and demonstrate the comparability of two different production batches of a therapeutic antibody for clinical phase II.

#### Solution provided by PPS

Protagen Protein Services has recommended and performed a comprehensive analytical concept consisting of two work packages.

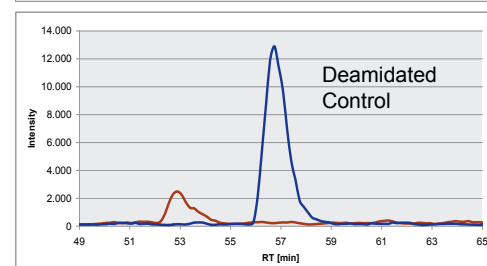
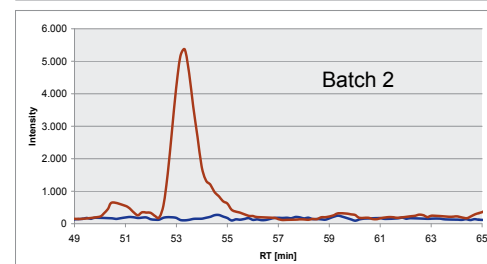
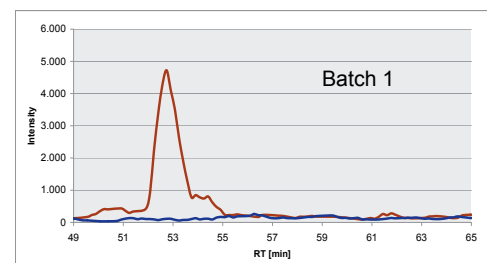
#### Work Package 1: Structural Characterization

- ▶ *N/C-terminal sequencing*
- ▶ *Peptide Mapping*
- ▶ *Total Mass*
- ▶ *Amino Acid Analysis*

#### Work Package 2: Impurity Analysis

- ▶ *Isoelectric focussing (IEF)*
- ▶ *Ion-exchange chromatography (IEX)*
- ▶ *Reverse Phase HPLC*
- ▶ *Identification of impurities (deamidation/Methion oxidation by MS)*

Comparability between the two different product batches of the therapeutic antibody was successfully demonstrated (see analytical example).



**Peptide Mapping by LC-MS for all potential deamidation sites shows comparability.**

(blue = deamidated, red = not deamidated peptide)

### Protagen Protein Services

A service provider fitting to your antibody development projects

Areas of Expertise	Track Record of Protagen Protein Services
<b>Regulatory Aspects</b>	<ul style="list-style-type: none"><li>▶ Data is already accepted by EMA, FDA, K-FDA from phase I projects up to market authorization</li><li>▶ Experienced with Biosimilars and New Biological Entities</li><li>▶ Frequent successful audits</li><li>▶ Full validation of state of the art equipment (GAMP 4 and 5)</li><li>▶ Efficient risk management system including in-house developed Software tools</li></ul>
<b>Analytical Aspects</b>	<ul style="list-style-type: none"><li>▶ Analyzing dozens of antibodies per year from international customers in all aspects of antibody structure</li><li>▶ Method development to release testing (GMP)</li><li>▶ World class experts in protein analysis with mass spectrometry experience since 1997</li><li>▶ Design of experiment-techniques and statistical analysis</li></ul>
<b>Customized Services</b>	<ul style="list-style-type: none"><li>▶ Flexible to fulfill your needs, including bidirectional method transfer</li><li>▶ We provide detailed quotations and transparent reporting</li><li>▶ We employ dedicated experts as project managers</li></ul>

To learn how Protagen Protein Services can help mitigate the risks in your antibody development process, please contact us today. Our experts are happy to discuss your analytical needs, without any obligation.



#### At Protagen Protein Services

Quality is one of the major pillars in the company's mission. It is an integral part of the company, also in non-GMP projects. It is based on a long standing scientific expertise.



# PROTAGEN

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