Menu Biopharmaceutical Analysis

Physicochemical Methods, Biochemical Methods, Immunological Methods, Assays for Biological Activity

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FEASIBILITY STUDIES, METHOD DEVELOPMENT AND VALIDATION
of mAb (IgG1-type) proteins

REMARKS:
• Work will be performed using qualified instruments and qualified staff.
• Feasibility studies are only done if required.
• For method development it is assumed that a successful feasibility study was performed before and that the methods will be validated for early phase GMP work (robustness studies are not required during an early phase validation).
• Full method validation will only be performed for methods which will be used in the scope of stability studies and release testing.
• Quality standard: Feasibility studies and method development are done under non-GMP (ISO 9001:2008). Method validation is performed under GMP.
• Reports: For setups no report will be written. The feasibility study includes writing of a short feasibility report. Method development includes writing of a SOP (status: non-validated). After finalization of method validation, SOP status: validated. The validation further includes writing of a validation protocol and report.

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<td>Content by UV</td>
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CHARACTERIZATION
of mAb (IgG1-type) proteins according to ICH guideline Q6B

REMARKS:
• Characterization will be performed based on generic methods for mAb/protein characterization.
• Methods will be specifically setup (optimized) for individual protein samples.
• Characterization will be performed using qualified instruments and qualified staff.
• Ph.Eur. will not be transferred, but product specific verification has to be performed.

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<tr>
<th>Test Item</th>
<th>Attribute</th>
<th>Additional Comments</th>
<th>Method</th>
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<td>Color of solution</td>
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<td>Ph.Eur. 2.2.2, USP</td>
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<td>General quality</td>
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<td>General quality</td>
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<td>Ph.Eur. 2.9.19a, USP</td>
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<td>Ph.Eur. 2.5.12</td>
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<td>Residual moisture by gas extraction</td>
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<td>Ph.Eur. 2.5.12</td>
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<td>Protein content by UV absorbance at 280 nm (simple sample prep)</td>
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<td>Size exclusion chromatography (SE-HPLC)</td>
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<td>Identity, purity, integrity</td>
<td>Aggregation, fragmentation</td>
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<td>Oxidation, variants</td>
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<td>Ion exchange chromatography (IEX-HPLC)</td>
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<td>Deamidation, heterogeneity (truncation, etc.)</td>
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<td>Amino acid sequence; disulfide bridges; free cysteines; truncation: N-terminal (pGln/Gln, pGlu/Glu) and C-terminal (±Lys); deamidation; oxidation; glycation; product related impurities; glycosylation site determination (PNGase F cleavage)</td>
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**STABILITY STUDIES AND RELEASE**

of mAb (IgG1-type), ADC (IgG1-type) and complex proteins

**REMARKS:**
- Potency assays should be part of the stability studies.
- Standard IgG1 type with complex type N-glycosylation at Asn297.
- Stability protocol will be provided by the customer.
- Setup will be performed.
- Transfer plan will be provided by the customer.
- Ph.Eur. will not be transferred, but product specific verification has to be performed.

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<td>Protein content by UV absorbance at 280 nm (simple sample prep)</td>
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<td>Bioassays (potency)</td>
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<td>Binding assays (ELISA)</td>
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<td>Size exclusion chromatography (SE-HPLC)</td>
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<td>● ● ● ●</td>
<td>Customer-specific</td>
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<tr>
<td>Reversed phase chromatography (RP-HPLC)</td>
<td>Identity, purity, integrity</td>
<td>● ● ● ●</td>
<td>● ● ● ●</td>
<td>Customer-specific</td>
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<td>Hydrodynamic interaction chromatography (HIC)</td>
<td>Identity, purity, integrity</td>
<td>● ● ● ●</td>
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<td>Customer-specific</td>
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<td>Ion exchange chromatography (IEC-HPLC)</td>
<td>Identity, purity, integrity</td>
<td>● ● ● ●</td>
<td>● ● ● ●</td>
<td>Customer-specific</td>
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<tr>
<td>Ion exchange chromatography (IEC-HPLC)</td>
<td>Identity, purity, integrity</td>
<td>● ● ● ●</td>
<td>● ● ● ●</td>
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<td>Peptide mapping RP-HPLC-UV</td>
<td>Identity, purity, integrity</td>
<td>● ● ● ●</td>
<td>● ● ● ●</td>
<td>Customer-specific</td>
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<tr>
<td>Capillary electrophoresis (CE-SDS reduced)</td>
<td>Identity, purity, integrity</td>
<td>● ● ● ●</td>
<td>● ● ● ●</td>
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<td>Capillary electrophoresis (CE-SDS non-reduced)</td>
<td>Identity, purity, integrity</td>
<td>● ● ● ●</td>
<td>● ● ● ●</td>
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<td>SDS-PAGE reduced</td>
<td>Identity, purity, integrity</td>
<td>● ● ● ●</td>
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<td>Customer-specific</td>
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<td>SDS-PAGE non-reduced</td>
<td>Identity, purity, integrity</td>
<td>● ● ● ●</td>
<td>● ● ● ●</td>
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<tr>
<td>Bioanalyzer (either reduced or non-reduced)</td>
<td>Identity, purity, integrity</td>
<td>● ● ● ●</td>
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<td>Capillary iso-electric focusing (cIEF)</td>
<td>Identity, integrity</td>
<td>● ● ● ●</td>
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<td>Molecular weight by mass spectrometry (reduced and non-reduced)</td>
<td>Identity, integrity</td>
<td>● ● ● ●</td>
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<td>N-terminal sequencing (Edman degradation)</td>
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<td>Amino acid analysis</td>
<td>Identity, concentration</td>
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<td>● ● ● ●</td>
<td>Ph.Eur. 2.2.56 (●) generic (●●)</td>
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<td>Monosaccharides (carbohydrate composition)</td>
<td>Identity</td>
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<td>Oligosaccharides (profile N-glycans)</td>
<td>Identity</td>
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<td>● ● ● ●</td>
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<td>Sialic acids (carbohydrate composition)</td>
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<td>● ● ● ●</td>
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<td>Asymmetric flow field flow fractionation (A4F)</td>
<td>Impurities (aggregates)</td>
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<td>● ● ● ●</td>
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<td>Light scattering by SEC-MALS</td>
<td>Impurities (aggregates)</td>
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<td>● ● ● ●</td>
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<td>Light scattering by DLS</td>
<td>Impurities (aggregates)</td>
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<td>Additives (e.g. preservatives)</td>
<td>Impurities</td>
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<td>● ● ● ●</td>
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<td>Residual Protein A (ELISA)</td>
<td>Impurities</td>
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<td>● ● ● ●</td>
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<td>HCP ELISA</td>
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<td>Impurities</td>
<td>● ● ● ●</td>
<td>● ● ● ●</td>
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<td>Western</td>
<td>Impurities</td>
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