TECHNICAL FACT SHEET

Developability Assessments of Protein Biopharmaceuticals

Health Inspired, Quality Driven.

Developability assessment or analytical profiling on a protein biopharmaceutical is executed in the beginning of the CMC - development to elucidate its suitability as a drug, that must fulfill certain quality criteria under terms of manufacturability, stability, physico-chemical and functional profile, as well as pre-clinical formulation. Developability assessment of protein biopharmaceuticals is considered as a de-risking strategy for the development of such molecules.

The objective is to identify potential critical quality attributes (CQAs), that influence the quality, potency, and manufacturability of the drug. Based on the experience of more than a decade of research in the field of developability studies, SGS Switzerland can offer several pre-defined packages of developability assessments, but also tailored approaches, specifically designed for the molecule of interest.

<table>
<tr><th>Analytical Approach</th><th>Analytical Technologies</th></tr>
<tr><td>Short-term stability studies:
<table>
<tr><td>T [C°]</td><td>0m</td><td>0.5m</td><td>1m</td><td>2m</td><td>3m</td><td>6m</td></tr>
<tr><td>2°-8°</td><td>x</td><td>x</td><td>x</td><td>x</td><td>x</td><td>x</td></tr>
<tr><td>25°</td><td>x</td><td>x</td><td>x</td><td>x</td><td>x</td><td>x</td></tr>
<tr><td>40°</td><td>x</td><td>x</td><td>x</td><td>x</td><td>x</td><td>x</td></tr>
</table></td><td>Analytics by: SEC-HPLC, cIEF, CE-SDS, DLS etc.
Propensity of the molecule to form HMW-species</td></tr>
<tr><td>Forced degradation: by low/high pH, photo-stress, chemical oxidatition, freeze/thaw cycles, shaking, thermal stress</td><td>High res. LC-MS/MS for peptide mapping from 50% to 100% sequence verification and PTM characterization (identification & level) available. Further analytical technologies available to assess charged variants, aggregates, etc.</td></tr>
<tr><td>Tests for function and specificity: as early as possible by binding-ELISA and later on by potency bio-assay.</td><td>MSD platform and any kind of standard read-outs available.</td></tr>
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Table1: Overview of Analytical Tests

First evaluation	Second check	Final analysis
Analysis of: Size distribution Formation of aggregates Discoloration Formation of particles **Method:** DLS SE-HPLC Color Turbidity Note: samples will be analyzed directly after pulling.	**Analysis of:** Charged variants Fragments Potency **Method:** cIEF CE-SDS SEC-MALS Binding ELISA/CBB Note: samples will be frozen after pulling and thawed for analyisis.	**Analysis of:** Amino acid sequence PTMs Intact mass Aggregates Hydrophilic and hydrophobic variants **Method:** PepMap LC-QTOF SEC-MALS RP-HPLC

Fig. 1: Stepwise approach of developability assessment.

Immunogenicity assessments

Based on 20 years of experience in this field, we can offer a package of in-vitro immunogenicity assessments, including cell-based in-vitro assays with monocyte-derived dendritic cells.
We can e.g. determine proinflammatory cytokines, as well as chemokines by using MSD Multiplex ELISA. Additionally, protein phosphorylation can be detected by homogenous AlphaLISA. At a later stage, either in pre-clinical or clinical trials, we can offer packages to determine anti-drug-antibody assays (ADA), including neutralizing antibody assays (NAB) for biopharmaceuticals.

PTM Characterization

With more than 30 years of experience in this area, we offer sequence verification through assignment confirmation using MS fragmentation data; PTM identification (and level evaluation) like deamidation, oxidation, isomerization, N-terminal glutamic cyclization, glycosylation, and many more.

Analytical Results Reports

The result of the developability assessment will be summarized in a report for the client, containing all relevant data and a conclusion.

SGS is your partner of choice when complex questions need to be answered. Our successful track record in the field of developability assessments gives your project the edge over your competitors.
Don`t hesitate to contact us and ask for your free quote today!

Contact information

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