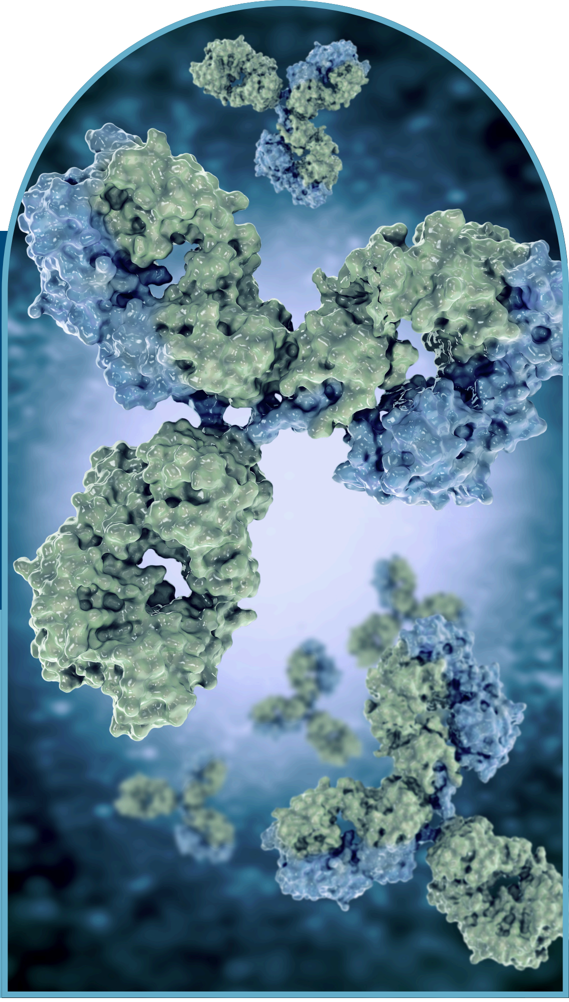
Beyond the Fold:

CONFIRMING STRUCTURAL CONSISTENCY WITH HDX-MS

High-Sensitivity Insight into Protein Structure During Process Comparability



As part of a process comparability exercise, a biopharma company needed to demonstrate that an optimized manufacturing process had no adverse effects on the structural integrity of their monoclonal antibody. While traditional tools like circular dichroism (CD) and differential scanning calorimetry (DSC) confirmed overall similarity, they lacked the sensitivity to detect subtle local changes in folding. To go beyond global assessments and gain deeper insight, the customer turned to Solvias for hydrogen-deuterium exchange mass spectrometry (HDX-MS)—a powerful method for evaluating higher order structure (HOS), which encompasses the secondary and tertiary folding of a protein.

THE CHALLENGES

- **Subtle Conformational Risk:** Process changes such as buffer modification or altered expression conditions can affect protein folding or flexibility—even when primary sequence and aggregation profiles remain unchanged.
- **Need for Localized Structural Clarity:** Standard HOS techniques deliver bulk measurements but cannot detect shifts in local dynamics or solvent accessibility.
- **Regulatory Scrutiny:** The process change supported a key regulatory filing, and definitive structural comparability data was required.

OUR COLLABORATIVE APPROACH

- **HDX-MS Platform Optimized for Monoclonal Antibodies:** Solvias applied its in-house generic HDX-MS method, requiring no assay development and enabling rapid turnaround.
- **Peptide-Level Resolution:** Using enzymatic digestion and mass spectrometry, Solvias mapped deuterium uptake across the molecule, identifying subtle differences in backbone hydrogen exchange patterns indicative of conformational change.
- **Advanced Kinetic Profiling:** By tracking deuterium uptake over multiple time points, the team could distinguish between transient flexibility and stable structural shifts—ensuring that folding behavior was fully understood.

THE RESULTS

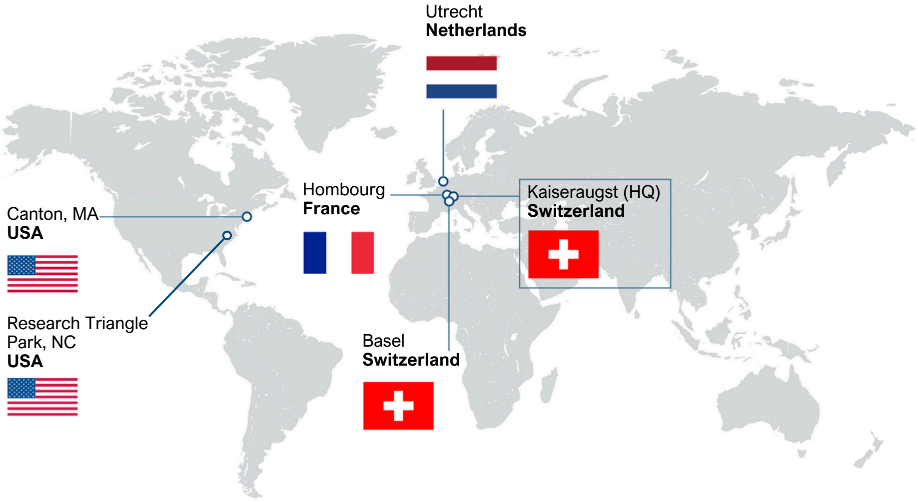
- No significant differences observed across process variants at the peptide level.
- Structural comparability confirmed with high sensitivity.
- Customer advanced regulatory submission with confidence.

CONCLUSION

HDX-MS offers unmatched sensitivity for detecting local structural differences, making it a powerful complement to traditional HOS tools like CD and DSC. It enables detailed comparability assessments, local conformational fingerprinting, and binding-site characterization—without requiring crystallization, tagging, or structural models. With its HDX-MS platform, Solvias helps customers see beyond the fold—delivering clarity where other methods reach their limits.

WHY PARTNER WITH US?

- CDMO/CRO
- Founded in 1999
- 800+ team members
- 175+ PhD-level scientists
- GMP, GLP, ISO9001 certified
- 22.5K sqm of lab capacity
- 700+ customers worldwide
- 6 centers of excellence



Contact us to speak with an expert: info@solvias.com

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