Navigating Stability Challenges in Protein Therapeutics

Tackling Unexpected Anomalies in Drug Development

During the lead candidate selection phase, an unexpected split peak was identified in the icIEF screening profile, raising concerns about the stability of the candidate molecules.

Key Challenge

The icIEF screening revealed a split main peak, indicating potential charge variant heterogeneity. This unexpected result suggested possible underlying chemical modifications, such as trisulfide bonds or free thiol groups, which could compromise the structural integrity and stability of the protein therapeutic, presenting significant challenges for its development and eventual commercialization.

Analytical Approach

To address this critical issue, the Intabio ZT system's advanced icIEF-UV/MS workflow was employed. This technology facilitated rapid, high-resolution analysis of charge variants, allowing for the direct correlation of pI shifts with changes in intact mass.

This approach allowed for the identification of trisulfide bonds and free thiol groups as the likely causes of the peak splitting, providing crucial insights into the molecular structure.

Impact

By identifying these molecular stability issues at an early stage, the progression of an unstable product was successfully halted, conserving significant time and resources. This early intervention ensured that development efforts were concentrated on candidates with the greatest potential for stability and efficacy, thereby optimizing the overall drug development pipeline and enhancing the likelihood of successful therapeutic outcomes.

Further insights and detailed analysis are available in our webinar re-broadcast. This event provides an opportunity to explore how advanced analytical techniques can transform drug development processes, ensuring the production of high-quality and stable biotherapeutic products. Attendees will gain valuable knowledge from leading experts in the field.

For details on the Intabio ZT system, visit:

How to Intabio resource hub

Intabio ZT system product page