## Stability modeling to predict vaccine shelf-life and evaluate impact of temperature excursions from the "cold chain"

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The stability of vaccines is of great interest industries and government institutions. Accelerated stability studies are designed to determine the rate of vaccine degradation over time as a result of exposure to temperatures higher than those recommended for product storage. However, commonly applied stability predictions based on application of zero- or first-order kinetics are very often too simplified for description of the degradation of biological products, which frequently undergo complex and multistep degradation reactions. We used an advanced kinetic approach mixing with statistical analysis to fit the forced degradation ELISA data by computed kinetic parameters, and finally, to predict valuable the long-term stability of vaccine containing several variants in a freeze-dried form. The modeling approach is based on the selection of the most appropriate kinetic equations which fit the degradation rate of compounds subjected to elevated temperatures, accelerating the rate of the reaction. According to 6 months data obtained at elevated storage temperatures, "two-step" models were identified to conveniently describe antigenicity of variants. We have predicted 2 years antigenicity, in agreement with real long-term stability data. The stability modeling procedure was also successfully applied for the prediction of antigenicity during several temperature excursions, thereby demonstrating the accuracy of the kinetic models. To the best of our knowledge, this is the first procedure mixing a global kinetic approach and modern statistical analyses to accurately determine a vaccine degradation rate able to predict shelf-life of bio-products stored in refrigerated condition and suffered temperature excursions from the cold chain.

### Speaker Biography

Didier Clenet has joined R&D Formulation and Stability platform of Sanofi-Pasteur in 2011. He focuses his work on high throughput screening formulations, stability prediction using advanced kinetics, vaccine activity structure relationship, particulate matter in vaccines and adjuvants process optimization and physio-chemical characterization. For more than 15 years in Sanofi R&D, he was dedicated on physical and biophysical characterization of active ingredients, freeze-dried products and monoclonal antibodies (mAbs, ADC). He developed novel X-ray diffraction and thermal analysis tools to study polymorphism and amorphous state in solid materials. His research interests are structural characterization and aggregation state determination using a variety of biophysical techniques (light scattering, flow-imaging, DSC and thermokinetics, fluorescence and infra-red spectroscopy). He implemented Biophysical lab and a lab-automation platform for bioproduct formulations. He is coaching to young scientists and performed courses in several Universities.

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