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Multi-attribute modelling for mRNA specification setting

A key challenge for mRNA vaccine and medicines development is represented by mRNA degradation under normal refrigerated storage condition (2-8℃). Product evolution over time is primarily driven by mRNA Integrity degradation, occurring mainly through chemical hydrolysis.
mRNA molecules are known to be particularly susceptible to hydrolysis under alkaline conditions, where degradation via backbone hydrolysis is accelerated. Consequently, understanding the impact of pH on degradation kinetics is critical for defining an appropriate control strategy.
A systematic investigation of pH effects on Integrity evolution was performed, to identify appropriate pH specification at release, assessing its impact both at release and in stability.
An enhanced Sestak-Berggren model was developed, including both temperature and pH effects to predict mRNA integrity degradation over time. A simulation approach was than developed to establish a quantitative linkage between pH and Integrity specifications at release and to compute pH impact on Integrity risk of out of specification at end of shelf-life. The results provide a scientifically justified framework to support definition of pH and Integrity product specifications.

Special/ Invited session

Classification

Both methodology and application

Keywords

Stability modelling, Specification setting, Simulation

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