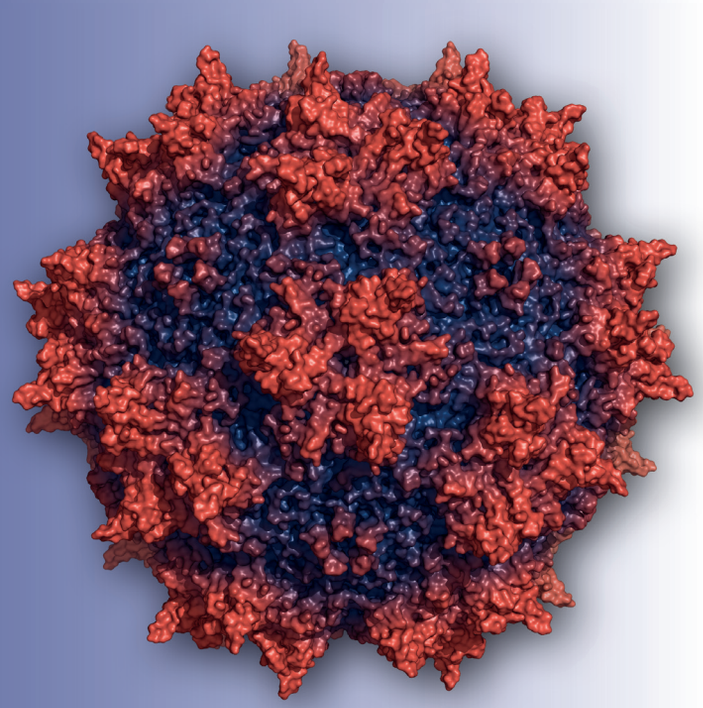
LEUKOCARE

formulation expertise meets data science

Stable formulations and robust analytics for viruses & viral vectors



IMPROVED STABILITY OF VIRUSES AND VIRAL VECTORS

Leukocare's formulation approach for viruses and viral vectors enhances long-term stability at higher temperatures while maintaining viral potency. Optimized formulations are designed by the synergistic combination of a data science based Design of Experiment (DoE) approach, molecular modeling, and an exhaustive database of regulatory approved excipients. This allows to explore the full design space, e.g. all possible excipients and combinations, and to benefit from Leukocare's extensive analytical expertise.

Benefits of Leukocare's formulation expertise:

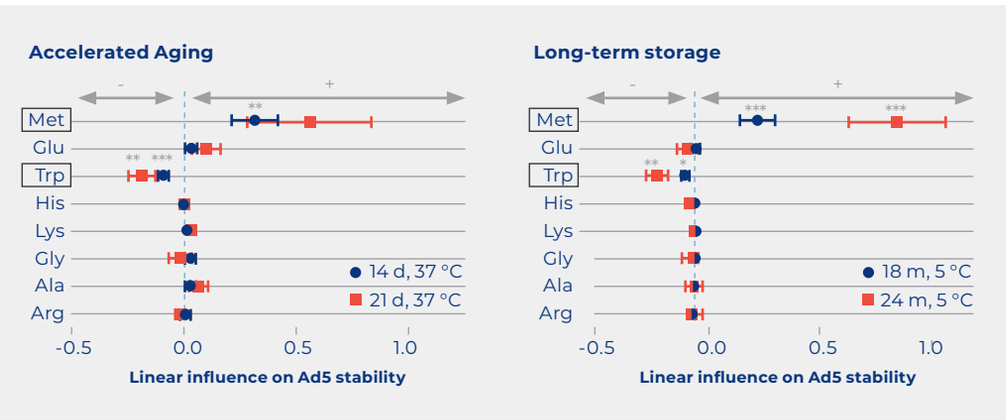
- Stabilize liquid or lyophilized formulations
- Reduce development time using data science
- Maintain viral stability and potency
- Handling of biological agents up to BSL-2

Tailored formulations to stabilize viral vectors

PBS is often used as the standard formulation buffer but has a number of significant drawbacks, which can cause problems during storage and in the clinics. Leukocare offers optimized buffers and enhances these by using its data science-based DoE approach to identify stabilizing excipients specific for each viral vector. The resulting tailored formulations ensure that viral stability and potency are preserved far beyond current standards.

Predictive power of accelerated aging enhanced by DoE for faster results

The combination of accelerated aging and DoE speeds up the formulation development process. Accelerated aging at higher temperatures can be used to predict the effects of long-term storage at low temperatures more quickly.

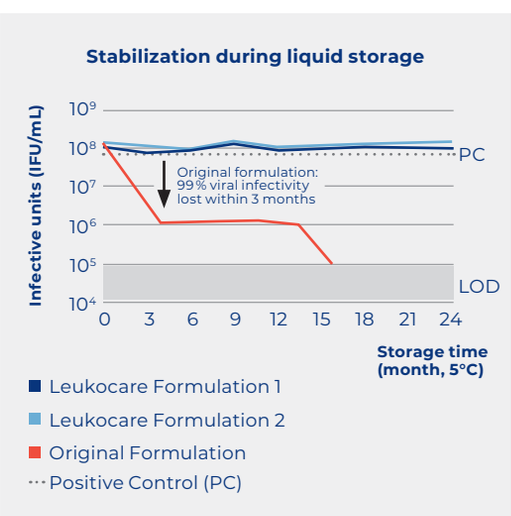


DoE based formulation development allows to apply regression analysis to statistically estimate the stabilizing effects of excipients. Accelerated aging at high temperature (37 °C, left) showed predictive power in detecting statistically significant ($p < 0.01$) stabilizing effects of methionine on the titer. This finding was confirmed by long-term storage at low temperature (5 °C, right). This indicates that accelerated aging combined with DoE provides reliable results to quantify excipient effects in a shorter period of time without compromising on quality.*

* Algorithm-Based Liquid Formulation Development Including a DoE Concept Predicts Long-Term Viral Vector Stability, Reinauer et al. (2020), Journal of Pharmaceutical Sciences

Maintaining viral potency during long-term liquid storage

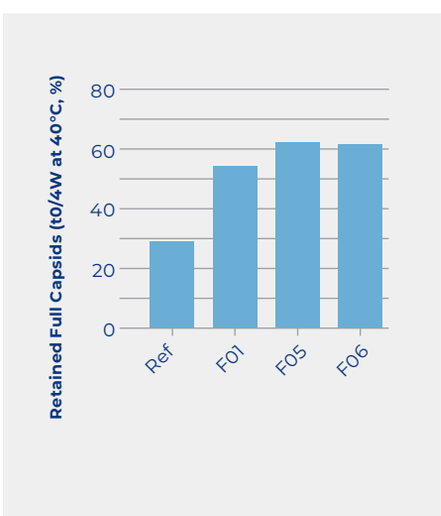
Stability and potency (infectivity) levels of most viruses decrease significantly during storage. To prevent this, virus preparations usually have to be stored frozen, requiring an uninterrupted cold chain and necessitating complex infrastructure. We developed stable liquid formulations that maintain viral stability and potency for 24 months at 5°C.



Comparison of infectivity of Ad5 between a commercially available formulation (red line) and two Leukocare formulations (blue lines). The original formulation lost 99% viral infectivity within 3 months, whereas the Leukocare formulations maintained viral stability and infectivity for 24 months at 5°C.

Preserve genome load of viral vectors

Sub-optimal formulation of non-enveloped viral vectors can result in instability of the capsid and leakage of the genome causing the drug product to be ineffective. Using Leukocare's formulation approach, the optimal combination of buffer and excipients reduced genome leakage at higher temperatures during accelerated aging experiments.



Amount of full capsids for AAV-2 in standard formulation buffer (PBS/0.001% Poloxamer 188, Ref) and 3 Leukocare formulations (F01, F05, F06) before and after storage at 40 °C for 4 weeks, measured by SEC-MALS. The Leukocare formulations show twice as many retained capsids after 4 weeks compared to the original standard formulation from the manufacturer.

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