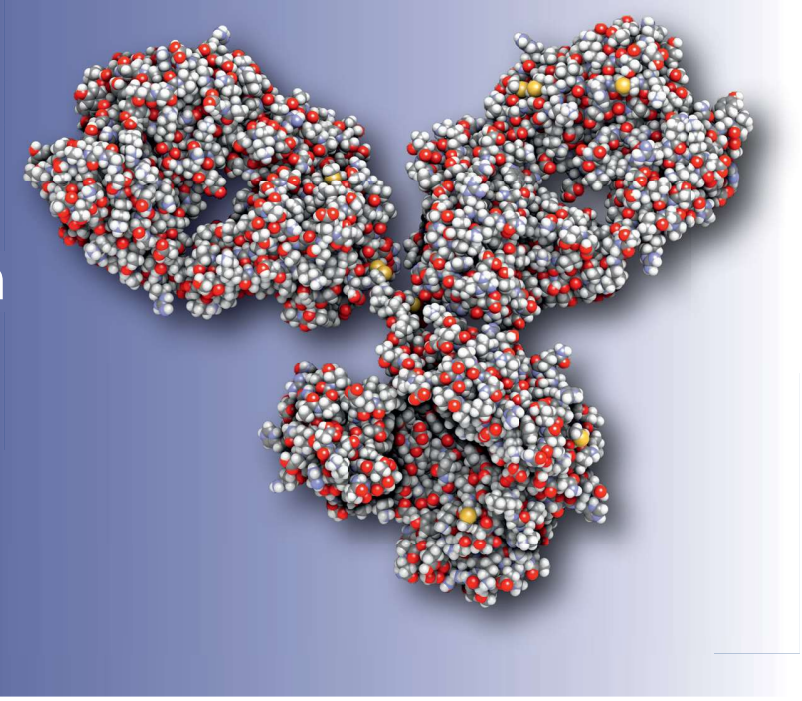
LEUKOCARE

formulation expertise meets data science

High concentration antibody formulation development



BENEFIT FROM STABLE FORMULATIONS WITH LESS VISCOSITY AND AGGREGATION

Work with the experts in high concentration antibody formulation

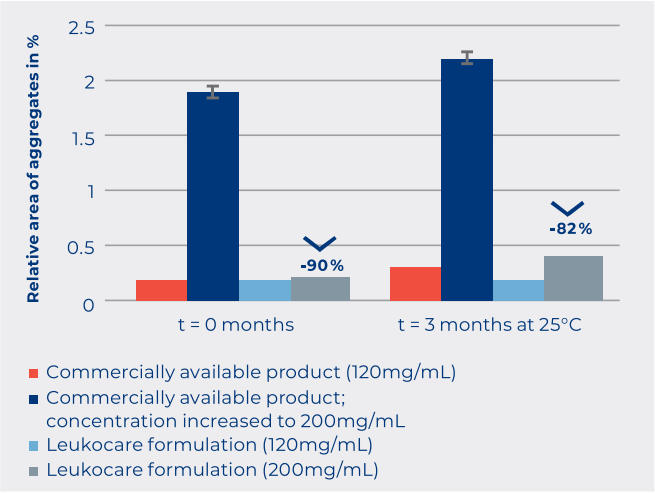
High concentration (HighCon) formulations can increase convenience for both the patient and doctor by using sub-cutaneous injection instead of IV, and lower the cost of administration, leading to higher commercial success. Achieving a stable and low viscosity antibody drug product at a high concentration can be very challenging. Leukocare's data science based Design of Experiment (DoE) approach using proprietary algorithms and in-depth formulation expertise combined with Leukocare's database of regulatory approved excipients enables for higher antibody concentrations while maintaining low viscosity.

Leukocare's high concentration antibody formulation expertise:

- Increase concentrations above 200 mg/mL
- Reduce aggregation
- Lower the viscosity for better injectability
- Improve long-term stability
- Decrease stress on the drug substance
- Co-formulation for multiple antibodies

Improved stability at almost 2x the antibody concentration

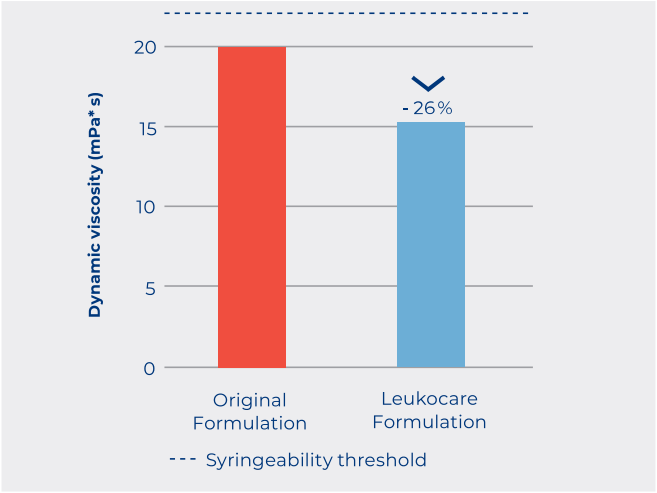
Up-concentrating an antibody using a standard formulation does not always result in a stable drug product. The up-concentrated commercially available formulation is significantly less stable as it results in a drastically increased rate of aggregation. In comparison, Leukocare's HighCon antibody formulation achieved a 2-fold higher concentration while stably preventing any increase in aggregate formation over time.



Leukocare's formulation of Trastuzumab achieves twice the original concentration without any loss in stability or increasing aggregation even after 3 months.*

Dynamic viscosity reduced with Leukocare HighCon antibody formulation

The viscosity of an antibody is a critical factor for a viable drug product. Conventional high concentration antibody formulations are often extremely viscous, inhibiting the ability for patient administration and thus commercial success. Using Leukocare's formulation technology, the regulatory approved excipient database, and data science based DoE approach allows high antibody concentrations while maintaining low viscosity.



The original formulation of Trastuzumab was up-concentrated to 220 mg/mL and resulted in viscosities which approached the syringeability threshold. With Leukocare's formulation, the dynamic viscosity dropped by 26%.*

*see Kemter et al. (2018), Biotechnol. J.

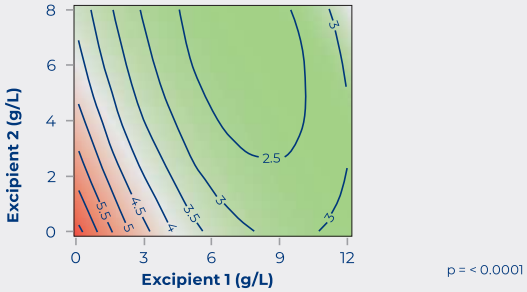
DoE and RSM for optimal formulations for High Concentration Antibodies

Finding the right combination of excipients, which results in low aggregation and low viscosity is essential for a successful drug product. To identify the optimal formulations, Leukocare employs a customized approach to the Design of Experiment (DoE) in order to estimate excipient interactions and determine their most stabilizing concentration. Using our data science know-how, we implement in-house algorithms to tailor the experimental design space based on the drug substance's unique biochemical and regulatory constraints.

In addition, DoE allows us to use the power of Response Surface Methodology (RSM) modeling to predict *in-silico* the composition of the most stabilizing, not yet tested formulations in the design space, reducing the amount of drug substance needed for *in-vitro* experiments and speeding up the formulation optimization process.

SEC: Abs. Delta Main Peak 1 after 4w at 40°C

Predicted Abs. Delta Rel. Area. Main Peak 1 [%]



We stabilized a bispecific antibody via optimization DoE at accelerated aging temperature. The contour plot shows the predicted sweet spot in the excipient design space corresponding to the smallest loss of the main peak by SE-HPLC. This allows refining the concentration selection for the best formulation candidate.

Excipient 1 (g/L)	Excipient 2 (g/L)	Buffer (g/L)	pH	Predicted Main Peak Loss [%]
11.0	12.6	32.5	6.0	0.93
10.8	18.4	33.5	6.3	0.69
10.1	24.2	34.2	6.4	0.47
9.4	29.0	34.8	6.4	0.26
9.0	32.7	35.1	6.5	0.07
8.8	**33.7**	**35.3**	**6.5**	**0.00**

Formulations gradient provided by the RSM technique on an optimization DoE for two excipients, buffer system and pH. The last *in-silico* predicted formulation on the gradient (in red) shows the highest stabilizing potential.

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