SCE 0611 Public Evidence Appendix

EV storage and stability

Literature review date: September 9, 2026

Controlling principle. EV shelf life is product-specific and must be demonstrated in the final formulation and container with stability-indicating assays; storage temperature alone cannot establish preserved quality.

Stability map

Domain	Primary concern	Evidence requirement
Temperature	Membrane integrity, cargo, aggregation, enzymatic activity, contaminant growth, and excursions can be temperature-dependent.	Evaluate the actual formulation, container, duration, handling, and relevant quality attributes.
Buffer composition	pH, ionic strength, osmolarity, excipients, and membrane interactions can change recovery or activity.	Formulation development should test compatibility, route, purity, sterility strategy, and stability.
Freeze–thaw cycles	Repeated freezing and thawing can alter size distribution, aggregation, membrane integrity, cargo, and potency.	Define freezing/thawing procedures and the maximum supported number of cycles.
Container effects	Adsorption, extractables/leachables, headspace, and container-closure integrity can affect recovery and quality.	Demonstrate compatibility in the final container-closure system.
Aggregation	Storage and handling can promote particle-particle association and alter apparent concentration or function.	Use stability-indicating size/aggregation measurements alongside other product attributes.
Sterility	Microbial contamination or compromised sterility can make a preparation unsuitable regardless of particle stability.	Maintain sterility assurance and relevant bioburden, endotoxin, mycoplasma, and closure controls.
Shelf life	Quality may change over time even under intended storage conditions.	Support expiration with real-time stability data for the exact product; accelerated studies are complementary.

Key evidence conclusions

Cold storage alone is not proof of stability. Identity, purity, potency, sterility, and other product-specific attributes must remain within justified acceptance criteria.

Stability-indicating assays must detect meaningful change. Particle count alone is insufficient; panels may include size distribution, aggregation, markers, purity, cargo, potency, pH, and appearance.

Shipping and handling are part of the stability program. Temperature excursions, vibration, agitation, delays, thaw rate, mixing, dilution, syringe residence, and filtration can affect quality.

Expiration dates require product-specific evidence. Claims of months or years of stability should identify formulation, container, storage conditions, tests, criteria, time points, and whether evidence is real-time or extrapolated.

Principal references

1. Théry C, Witwer KW, Aikawa E, et al. Minimal information for studies of extracellular vesicles 2018 (MISEV2018). J Extracell Vesicles. 2018;7:1535750.

2. Welsh JA, Goberdhan DCI, O'Driscoll L, et al. Minimal information for studies of extracellular vesicles (MISEV2023): From basic to advanced approaches. J Extracell Vesicles. 2024;13:e12404.

3. Jeyaram A, Jay SM. Preservation and storage stability of extracellular vesicles for therapeutic applications. AAPS J. 2018;20:1.

4. Kusuma GD, Barabadi M, Tan JL, Morton DAV, Frith JE, Lim R. To protect and to preserve: novel preservation strategies for extracellular vesicles. Front Pharmacol. 2018;9:1199.

5. Relevant biological-product stability, sterility, container-closure, and manufacturing guidance applied according to product class and jurisdiction.