SCE 0610 Public Evidence Appendix

EV potency and dose

Literature review date: September 9, 2026

Controlling principle. EV dose is not a universal physical quantity; a defensible dose connects a defined product measurement to biological potency, exposure, safety, and indication-specific evidence.

Dose and potency map

Domain	What is measured	Interpretive boundary
Particle number	Detectable particles in the administered preparation	Count depends on analytical platform and includes no guarantee of EV identity, purity, cargo, or activity.
Protein quantity	Total measured protein mass	Includes EV-associated proteins plus potentially co-isolated soluble proteins, aggregates, lipoproteins, and contaminants.
Cell-equivalent dose	EV output normalized to a defined number of producer cells	Manufacturing yield does not establish the amount or activity of the final administered product.
Cargo-based dosing	Amount of a selected RNA, protein, lipid, or other cargo	Cargo quantity becomes biologically meaningful only if localization, delivery, target engagement, and activity are demonstrated.
Functional assays	Biological response produced by a defined amount of product	Assay relevance, specificity, reproducibility, and relationship to the intended mechanism and clinical effect must be established.
Dose-response testing	Relationship between administered amount/exposure and measured response	Can identify minimally active ranges, plateaus, saturation, toxicity, and response variability for the actual product.
Universal dosing standards	Cross-product dose equivalence	No universal EV dose unit exists; nominal doses should not be transferred across non-equivalent products.

Key evidence conclusions

Quantity and potency are different. A larger amount of poorly active or contaminated material is not equivalent to a smaller amount of a more active preparation.

Dose identity must be explicit. A reported dose should state what was measured, the method, units, sample preparation, and whether the value describes the final administered product.

Route changes exposure. Intravenous, local, intra-articular, inhaled, topical, and other routes can produce different biodistribution and target-tissue concentrations from the same nominal dose.

Repeat dosing adds a time dimension. Dosing interval, accumulation, clearance, immune responses, and changing recipient biology mean cumulative dose alone does not define temporal exposure.

Principal references

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3. Witwer KW, Van Balkom BWM, Bruno S, et al. Defining mesenchymal stromal cell (MSC)-derived small extracellular vesicles for therapeutic applications. J Extracell Vesicles. 2019;8:1609206.

4. Gimona M, Brizzi MF, Choo ABH, et al. Critical considerations for the development of potency tests for therapeutic applications of mesenchymal stromal cell-derived small extracellular vesicles. Cytotherapy. 2021;23:373-380.

5. International Society for Extracellular Vesicles and relevant biological-product guidance concerning EV dose reporting, potency, characterization, and clinical translation.