

In Vitro Drug Release: Separate Release from Test Artifacts

RUIKANG Li (Neo)

Hongkong Kannry Industrial Co., Ltd. | www.kannrybio.com

Abstract. A release curve combines material behavior with solubility, sampling, stability and apparatus effects. This guide focuses on drug-specific controls, including dialysis transport, and shows when a measured medium concentration is insufficient to claim sustained release.

Keywords: drug carrier; release; sink capacity; dialysis; mass recovery

1. Define the reported fraction

Specify whether the result is dissolved parent drug in the vessel, drug reaching a dialysis receiver or another operational fraction. Use an independently assayed initial payload in the tested material as the percentage denominator.

Record medium composition, volume, mixing, temperature, sampling location, separation, replacement and sample storage. Conditions must be selected for the actual drug-carrier combination; this document is not a universal release protocol.

2. Assess sink capacity

A conventional screening ratio is $V \times C_s / M_0$, where C_s is equilibrium solubility in the test medium and M_0 is the assayed initial payload. A ratio of at least 3 is a common sink convention [1].

Example: $C_s = 0.50$ mg/mL, $M_0 = 4.00$ mg and $V = 10.0$ mL give a ratio of 1.25. A volume of 24.0 mL gives 3.0. These hypothetical values are not a prescribed medium volume.

Verify solubility and stability under actual conditions. Added surfactant or a changed pH may alter both drug solubility and the carrier response.

5. Correct sampling and retain a recovery trail

For a well-mixed vessel of constant volume V , drug-free replacement after each sample and concentrations measured immediately before withdrawal: cumulative recovered drug at point $n = V \times C_n + \text{sum of } (v_i \times C_i)$ for all earlier samples. Include analytical dilution corrections first. The current aliquot is already included in $V \times C_n$.

3. Challenge dialysis transport

A receiver curve includes both departure from the carrier and transport across the membrane. Membrane cutoff and concentration gradients can affect apparent kinetics [2].

Run a free-drug transport control with matched membrane, volumes and conditions. Evaluate membrane adsorption, particle retention and compartment mixing. A slow receiver curve alone is not proof of slow release from the material.

4. Investigate a low plateau

Run drug-only stability/recovery controls through vessels, filters and storage. Test unloaded carrier with drug when re-adsorption is plausible. Demonstrate assay selectivity; assess matrix effects and use matrix-matched calibration where justified [3].

At the endpoint, assess residual drug on the solid and relevant apparatus losses. Low medium recovery may reflect retained drug, degradation, precipitation or analytical loss. Do not assign a mechanism from curve shape alone.

Report independent profiles and uncertainty. A fitted kinetic model does not independently establish a release mechanism or predict clinical performance.

Sampling condition	Calculation / record	Limit
Partial replacement	$V = 10.0$ mL; earlier aliquots = 1.0 mL; $C_1 = 0.10$, $C_2 = 0.20$, $C_3 = 0.25$ mg/mL. $M_3 = 2.80$ mg.	For 4.00 mg payload: 70.0%, not 62.5%.
No replacement	Use actual remaining pre-sampling volume, plus mass in earlier aliquots.	Track losses from evaporation separately.
Complete exchanges	Sum recovered mass in each collected interval.	Account for retained liquid and incomplete collection.
Dialysis	Free-drug transport, membrane recovery and particle-retention controls.	Receiver appearance may be membrane-limited.
Endpoint	Residual solid extraction, medium recovery and apparatus recovery.	Do not equate missing drug with sustained release.

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6. Decision for comparing candidates

Keep medium chemistry and operational definitions comparable. If recovery, solubility or membrane controls fail, investigate the method before ranking carriers. The sampling correction is a conservation-of-mass tool; it does not restore degraded drug or unmeasured adsorbed material.

Relation to the existing series

KB-TG-020 covers elemental inventory during material immersion. This guide adds drug-specific stability, sink-capacity and membrane-transport controls. Neither medium recovery nor a release curve is a clinical efficacy claim.

References and evidence boundaries

[1] FDA. Compilation of FDA Guidance and Resources for in vitro Dissolution Testing of Immediate Release Solid Oral Dosage Forms. Date not stated. Official FDA resource. Sink convention only; oral-dosage acceptance criteria are not transferred to mineral carriers.

[2] Moreno-Bautista G, Tam KC. Evaluation of dialysis membrane process for quantifying the in vitro drug-release from colloidal drug carriers. Colloids Surf A. 2011;389:299–303. doi:10.1016/j.colsurfa.2011.07.032. Published 20 September 2011.

[3] FDA / ICH. Q2(R2), Validation of Analytical Procedures. March 2024. Official guidance PDF. Principles of matrix-appropriate assay evaluation.

Sources checked 30 October 2026. Research planning guidance only; no Kannrybio lot-performance, clinical or regulatory-approval claim.

Prepared by: RUIKANG Li (Neo)



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