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WHITE PAPER

IMPACT OF THE RAYDYLYO® DEVICE ON PRIMARY DRYING EFFICIENCY IN FREEZE-DRYING: COMPARATIVE STUDY ON 2.3% MANNITOL IN DIFFERENT VIALS SIZE AND CONFIGURATIONS

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Impact of the RayDyLyo® Device on Primary Drying Efficiency in Freeze-Drying: Comparative Study on 2.3% Mannitol in different vials size and configurations

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1. Executive Summary

This white paper gathers preliminary results from a study on the impact of RayDyLyo® on the primary drying performance of a standard lyophilization cycle applied to several configuration of vials and stoppers. The strongest result was obtained with RayDyLyo® combined with a serum stopper, which reduced primary drying time by 21.9% versus the conventional semi-stoppered reference in 4R vials and reached a vial-specific sublimation rate of 0.084 g/vial.hour, essentially matching the naked-vial reference at 0.085 g/vial.hour.

The study also shows that RayDyLyo® performance depends on the configuration. In 4R, 6R and 10R, the serum stopper remained the best RayDyLyo® option relative to the lyo stopper, confirming that stopper choice is a key lever. These additional results support the conclusion that the serum-stopper configuration is the preferred design when aiming to maximize primary drying performance while using RayDyLyo®.

Naked vials were included as a reference to position the RayDyLyo® results against a condition with minimal stopper-related resistance. This comparison is especially valuable for the 4R data because it shows how closely the best RayDyLyo® configuration approaches the drying behavior of an unstopped vial.

For 4R vials, RayDyLyo® clearly improved primary drying performance relative to the conventional reference. RayDyLyo® with lyo stopper reduced primary drying time by 9.6%, while RayDyLyo® with serum stopper reduced it by 21.9%. In practical terms, this means that for low vial-specific sublimation rates in the range observed here, the RayDyLyo® serum-stopper configuration provides a strong performance advantage.

The 6R and 10R results support the same ranking of configurations. In 6R, RayDyLyo® with serum stopper improved primary drying by 13% versus the configuration with lyo stopper. In 10R, the serum stopper still outperformed the lyo-stopper version by reducing the primary drying by 7%. These supporting data reinforce that the serum stopper is the best-performing RayDyLyo® configuration.

The 4R nested results show no negative impact of the nest on primary drying performance. On the contrary, the best nested 4R configuration reached 1401 minutes, corresponding to a 22.9% reduction versus conventional and essentially the same performance as naked vials at 1419 minutes. This is an important result because it means that nesting can be retained for automation, ease of transport, and operational simplicity without sacrificing primary drying efficiency.

Beyond drying performance, the nested RayDyLyo® approach also supports manufacturing operations by facilitating vial handling, improving transport robustness, and eliminating the need for subsequent crimping after the lyophilizer. This combination of primary drying performance and operational benefit is particularly attractive for clients seeking a ready-to-use, automation-friendly solution.

The benefit appears strongest at lower vial-specific sublimation rates. In the 4R study, the best RayDyLyo® configurations operated around 0.084 to 0.086 g/vial.hour, whereas the less favorable larger-format conditions moved toward approximately 0.13 g/vial.hour and above. The nesting results also suggest that nest geometry and the amount of plastic material matter, likely through their influence on glass-vial exposure to gaseous conduction and therefore on efficient heat transfer during primary drying.

Overall, the data position the 4R RayDyLyo® serum-stopper configuration as the leading option in this study:

1. superior primary drying performance,
2. no loss of cake quality,
3. no negative impact from nesting,
4. and clear manufacturing-process advantages.

The document below is therefore organized around three themes: the superiority of RayDyLyo® with serum stopper, the impact of the nest, and the broader impact of RayDyLyo® on manufacturing performance.

2. Introduction

Freeze-drying remains one of the most widely used technologies for stabilizing sensitive biopharmaceutical, diagnostic and small-molecule formulations. As manufacturing facilities increasingly adopt automated and intervention-free processes, container–closure systems (CCS) must evolve to support both regulatory expectations (EU GMP Annex 1 revision, reduction of Grade A human interventions) and operational efficiency.

RayDyLyo® is an all-plastic, pre-assembled, push-fit capping system designed to simplify vial closure by eliminating the traditional post-freeze-drying crimping step. By integrating the stopper directly within the plastic cap, RayDyLyo® enables a fully RTU (Ready-To-Use) workflow and facilitates automation in aseptic operations. However, compared to conventional semi-stoppered vials, RayDyLyo® introduces additional components around the stopper that could influence heat and mass transfer during freeze-drying.

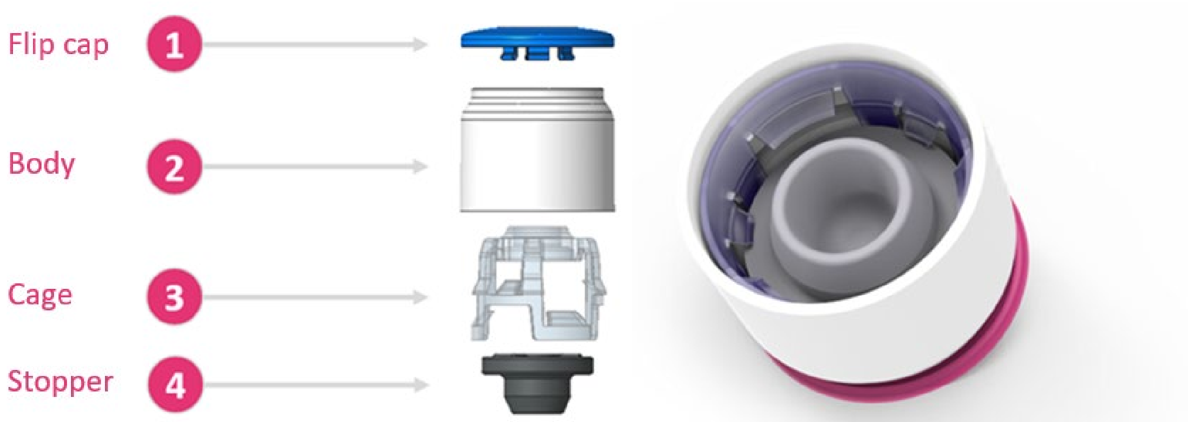


Figure 1: Illustration of RayDyLyo® components with pre-assembled stopper

From a freeze-drying perspective, several parameters govern primary drying performance, including:

- The geometry of the venting pathway and in particular the solvent vapor transfer surface left by the stopper
- Free vapor flow space between vials within the load
- The vial heat transfer coefficient (Kv), which determines energy input to the frozen product and could be impacted by the Nesting of the vials

Because RayDyLyo® adds mechanical structures around the stopper, its influence on local vapor flow dynamics needs to be experimentally assessed. Theoretical considerations suggest two opposite effects may occur:

1. Increased steric hindrance, potentially slowing sublimation by restricting vapor escape in specific vapor sublimation conditions
2. Greater spacing between vials, potentially facilitating vapor circulation and reducing inter-vial shielding

To date, however, no quantitative study has been performed to evaluate the influence of RayDyLyo® on primary drying behavior under controlled conditions.

The objective of this white paper is to present the results as the central proof point for RayDyLyo® performance in freeze-drying and to translate these data into practical messages for potential users. The document is structured around three questions: first, why RayDyLyo® with serum stopper is the best-performing configuration; second, how the nest influences primary drying and handling; and third, how RayDyLyo® can improve the overall manufacturing process. The 6R and 10R data are included only as supporting evidence to confirm the ranking of configurations, while keeping the emphasis on simple, user-relevant performance indicators such as relative primary drying time and vial-specific sublimation rate.

- With lyo or serum stoppers, enabling exploration of the role of stopper type.
- Naked on a lyo tray versus nested vials and RayDyLyo® nested ("Sandwich" configuration)

3. Materials and Methods

3.1. Equipment

All experiments were conducted using a Lyostar™ 3 freeze-dryer (SP Scientific, USA), with a total chamber volume of 0.113 m^3, three shelves of 1,394 cm^2 each and a condenser capacity of ~30 L with a surface area of 5,481 cm^2. The unit is equipped with:

- Capacitance manometers (MKS) for absolute pressure measurement
- Pirani thermal conductivity gauges for pressure measurement and for determination of the endpoint of primary drying (see Figure 4)
- A front observation window enabling real-time visual check of the load

Pressure readings from both Pirani and MKS gauges were used to determine the transition point marking the end of primary drying, following common industry practice for conservative cycles in excipient-only loads[1]

3.2. Container and Closure System configurations tested

All vials used in the study were 4R, 6R and 10R Schott Fiolax® Type I clear tubular glass vials.

For each volume, 3 CCS configurations were evaluated:

1. Conventional reference
    - 4R vial with 13 mm bromobutyl lyo stopper (Aptar)
    - Semi-stoppered configuration
2. RayDyLyo® configuration A
    - RayDyLyo® cap with bromobutyl lyo stopper pre-assembled in the device
3. RayDyLyo® configuration B
    - RayDyLyo® cap with bromobutyl serum stopper pre-assembled in the device

On top of this, for the 4R configuration two extra configurations have been tested:

4. Nested vials with RayDyLyo®
5. Nested vials with Nested RayDyLyo® ("sandwich" configuration) with one traditional Nest and one new Ecodesign Nest (developed by ARaymond to diminish the carbon footprint of its solution)

[1] Patel SM, Doen T, Pikal MJ. Determination of end point of primary drying in freeze-drying process control. AAPS PharmSciTech. 2010 Mar;11(1):73-84. doi: 10.1208/s12249-009-9362-7. Epub 2010 Jan 8. PMID: 20058107; PMCID: PMC2850457.

All RayDyLyo® units were supplied as Ready-to-Use (RTU) components.

To have a more comprehensive set of data, for each vials size, the completely naked vials (without stopper) have been lyophilized.

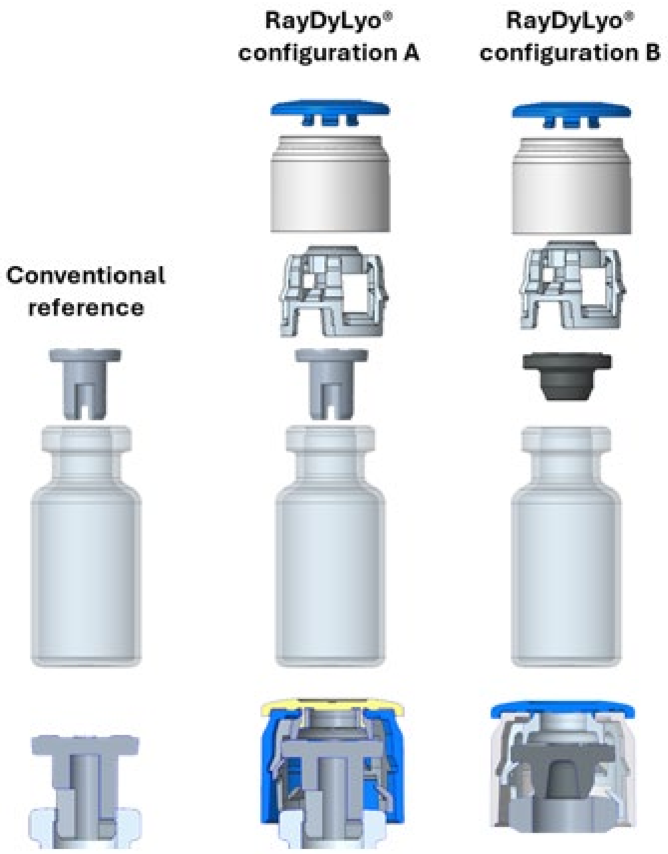


Figure 2 : Illustrations of CCS configurations

3.3. Formulation and Filling process

A 2.3% (w/v) Mannitol solution (Mannitolum Ph. Eur., GMP grade, Fagron) was prepared using ultrapure water. The formulation was chosen as a standard bulking agent representative of excipient-only development studies[2], providing a robust Freeze-dried cake with elegant appearance.

  - Target fill volume per vial: 4R: 2.0 mL; 6R: 3.0 mL; 10R: 5.0 mL
- Weighing equipment:
  - Sartorius MSA125P-100-DA for excipient
  - Sartorius MSA12201S-000-DO for solvent and compounding bottle
- Filling tools: Rainin Pipet-Lite micropipettes with BioClean Ultra tips

[2] Mannitol as an Excipient for Lyophilized Injectable Formulations Thakral, Seema et al. Journal of Pharmaceutical Sciences, Volume 112, Issue 1, 19 - 35

For each configuration, 75 vials were filled and arranged uniformly on a freeze-drying tray or in the nests (for 4R vials). Vials were semi-stoppered with either the conventional lyo stopper or the fully assembled RayDyLyo® devices. Three Pt100 temperature probes were inserted into representative vials positioned at the center and edges of the load.

3.4. Freeze-drying cycle

A freeze-drying cycle was applied identically to all configurations. Cycle parameters are summarized in Table 1.

Table 1: Lyophilisation recipe applied to every configuration tested

	Step	Temperature (°C)	Pressure (µBar)	Time (Hr)
1	Entry samples tray	Room Temperature	Atm	0
2	Freezing	-40	Atm	1
3	Plateau	-40	Atm	3
4	Primary Drying	-10	150	6
5	Primary Drying	-10	150	30*
6	Secondary Drying	-10	maximum	2
7	Secondary Drying	10	maximum	2
8	Secondary Drying	10	maximum	6
9	Sterile Nitrogen filling	5	Atm	NA
10	Stoppering	NA	Atm	NA
			Total Maximum Duration :	50

*corresponding to the maximum duration of step 5 as during the primary drying, the Pirani and MKS pressure reading will be checked and the step 5 will be shortened by switching to step 6 as soon as the two pressure curves gather and equilibrate

The cycle was designed to:

- ensure no risk of collapse for a 2.3% Mannitol formulation in conventional configuration
- maintain stable product temperatures well below the critical temperatures for the duration of the sublimation phase
- facilitate comparative assessment of sublimation kinetics independent of formulation risk

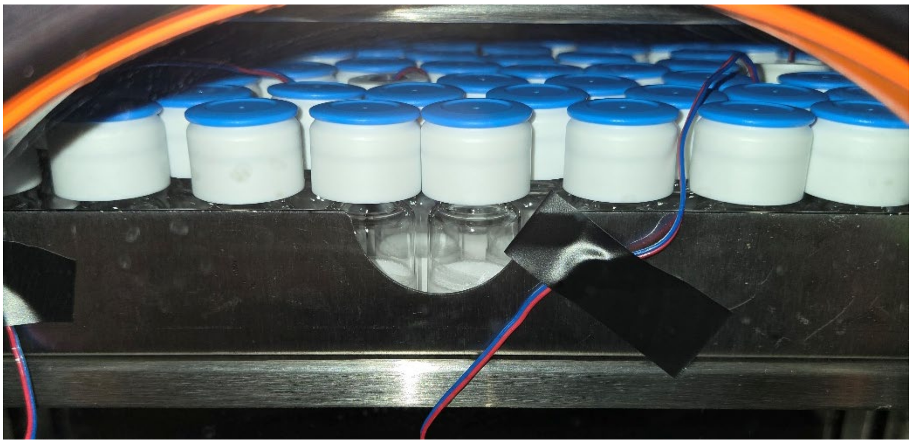
The end of primary drying was determined by inspection of the convergence between Pirani and MKS pressure curves, marking the onset of desorption when vapor flow decreases below the detection threshold of the Pirani gauge.

3.5. Lyophilization process monitoring

The following parameters were continuously monitored:

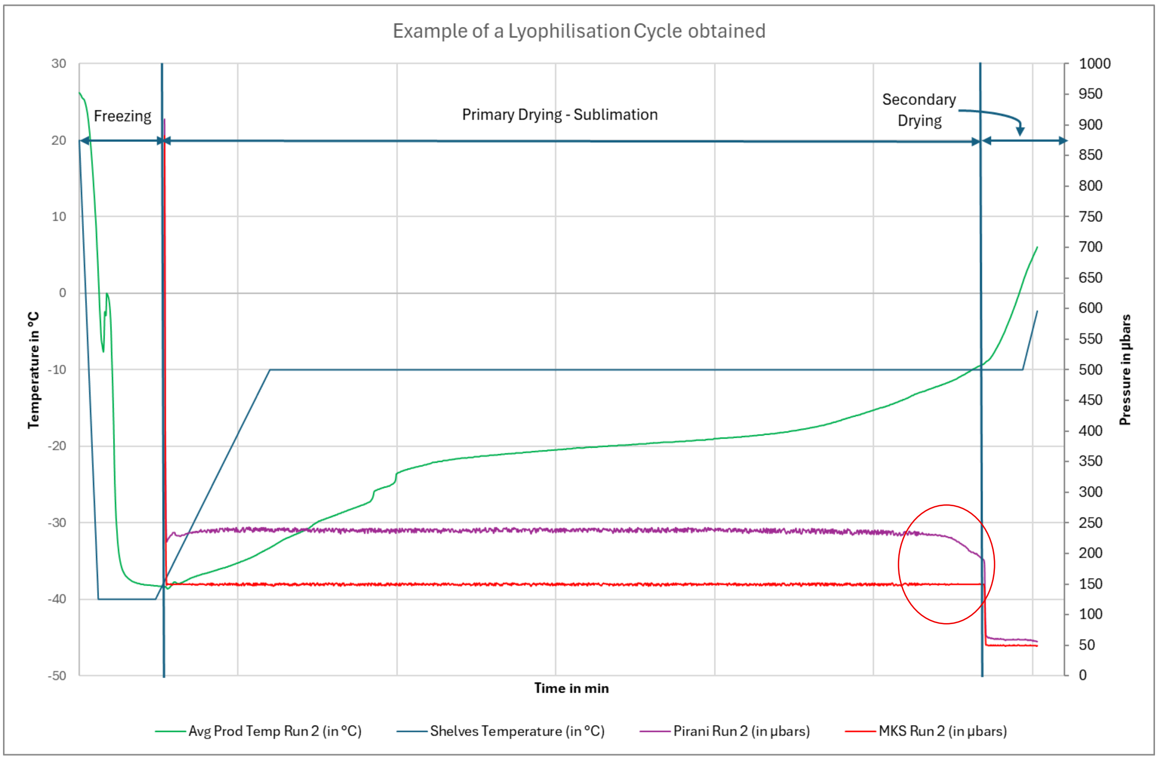
- Chamber pressure
- Shelf temperature
- Product temperature via Pt100 probes
- Time to convergence of pressure readings (MKS and Pirani)
- Visual check of the load at key stages (see Figure 3):
  - End of freezing
  - Early primary drying
  - Apparent end of primary drying defined by the convergence of the Pirani and MKS readings

Figure 3 Picture of the vials seen through the observation window of the lyo chamber (load of 6R vials with their RayDyLyo® device on)



Primary drying duration was calculated as the elapsed time between the start of sublimation and the Pirani/MKS convergence point as illustrated on the Figure 4.

Figure 4: Example of a typical lyophilisation graph and information used for the determination of Primary drying duration



The end of primary drying in this study was determined using Pirani/MKS convergence, a non-invasive well-accepted method. While robust and appropriate for comparative work, this approach carries inherent scientific limitations that should be acknowledged to support correct interpretation of the results:

- The Pirani gauge is sensitive to gas composition, reading higher when water vapor dominates.
- As sublimation slows and nitrogen becomes the main gas, the Pirani signal converges with the MKS capacitance manometer.
- This represents the point where water vapor from sublimation flux becomes negligible, not the absolute cessation of sublimation.

Therefore, the endpoint is a practical and conservative approximation, not a direct measurement of complete water removal. It is nevertheless fully valid for comparative analysis, since all configurations use the same rule.

Additionally, the freeze-drying cycle applied here was intentionally conservative to ensure product robustness:

- low shelf temperature,
- cautious pressure setpoint,
- long maximum primary drying step,
- operation far below Mannitol critical temperatures at key stages (Total Solidification Temperature, Tg' and others)

Therefore, the absolute durations may exceed the true sublimation requirement but differences between CCS configurations remain meaningful and comparable. It was still affording a relatively significant vial specific sublimation rate at around 0.14 g/vial.hour for the 10R configuration

The present study aims to compare relative performance between CCS designs, not to establish the minimum cycle duration.

Thus, Pirani/MKS convergence was deemed appropriate for:

- comparing drying kinetics,
- thus evaluating mass-transfer effects of the different CCS configurations,
- ensuring identical endpoint criteria across configurations.

In our study, it is not intended for:

- defining absolute primary drying times,
- optimizing shelf temperature or pressure

3.6. Post-drying evaluation

After unloading, all vials were visually evaluated using a predefined scale (Grades A to G) adapted from standard freeze-drying cake appearance criteria (Table 2) Grade A corresponds to a uniform, self-supporting cake adhering to the bottom of the vial.

Table 2: Appearance Criteria for the lyophilisation cakes appearance

Grade	Appearance
A	Firm cake adhering to the bottom of the vials
B	Non-uniform cake with a crust or glaze
C	Cake with a poor self-supporting structure
D	Partially collapsed cake
E	Melt-back
F	Disappearing cake
G	Puffing

Only visual check was performed as part of this preliminary study. Critical quality attributes such as residual moisture, reconstitution time, or structural analysis were considered out of scope but are candidates for future follow-up investigations.

4. Results

4.1. Overview

The results are presented here with a primary focus on 4R vials as generating the clearest evidence of performance improvement with RayDyLyo®. The central result is that RayDyLyo® with serum stopper outperformed both the conventional semi-stoppered configuration and the RayDyLyo® lyo-stopper configuration, while nested 4R formats confirmed that these gains can be preserved in an automation-friendly presentation.

Across all tested conditions, all cakes remained Grade A. This outcome is showing that the observed gains in primary drying performance were not achieved at the expense of visible product quality.

4.2. Primary drying duration and Sublimation performance

Primary drying duration was determined for each test run based on the inflection point where the Pirani and MKS pressure readings converged, indicating a reduction in vapor flow and marking the transition to secondary drying.

Table 3 summarizes the primary drying durations for the 4R configurations tested and the corresponding vial-specific sublimation rates for each CCS configuration tested.

Table 3: 4R Duration of Primary drying and Vial Specific Sublimation rates calculated for the different experiment performed

Design	Vial Size (in ml)	RayDyLyo® diameter (in mm)	Stopper type	Duration of the primary drying (in min)	Vial specific Sublimation rate (in g/vial.hour)	% variation compared to conventional (in %)
Naked vial	4	NA	NA	1419	0.085	-21.9
Conventional	4	NA	Lyo	1818	0.064	0
RayDyLyo®	4	13	Lyo	1644	0.073	-9.6
RayDyLyo®	4	13	Serum	1420	0.084	-21.9
Nested vials (Nest B*) +RayDyLyo®	4	13	Serum	1537	0.078	-15.4
Nested Vials (Nest A*) + RayDyLyo (®)	4	13	Serum	1401	0.086	-22.9
Nested vials (Nest B*) + Nested RayDyLyo®	4	13	Serum	1490	0.080	-18.0
Nested vials (Nest B*) + Nested RayDyLyo® Ecodesign	4	13	Serum	1520	0.079	-16.4

***Vials Nests A and B are sourced from 2 different suppliers but are both compatible with the same configuration of Nested RayDyLyo® both using the same serum stopper**

Interpretation

- For 4R vials, RayDyLyo® improved primary drying in both tested stopper configurations, with the serum stopper delivering the strongest result.
- RayDyLyo® with serum stopper reduced primary drying time by 21.9% versus conventional and reached a vial-specific sublimation rate of 0.084 g/vial.hour.
- This performance is essentially equivalent to the naked-vial reference at 0.085 g/vial.hour, showing that the best RayDyLyo® 4R configuration behaves nearly like an unstopped vial from a mass-transfer perspective.
- The nested 4R results confirm that nesting does not create a penalty; the best nested condition reached 1401 minutes and a 22.9% reduction versus conventional.
- Differences between nests suggest that nest geometry and plastic quantity matter, likely because they affect glass exposure and heat transfer conditions.

The 4R data therefore support a very clear message: when used with a serum stopper, RayDyLyo® is not only compatible with efficient primary drying, but can outperform the conventional reference while preserving the operational advantages of the platform.

Table 4 summarizes the primary drying durations for the 6R and 10R configurations tested in order to compare the relative effect of the type of stopper (lyo vs serum) in RayDyLyo® and the corresponding vial-specific sublimation rates for each CCS configuration tested.

Table 4: 6R and 10R Duration of Primary drying and Vial Specific Sublimation rates calculated for the different experiment performed

Design	Vial Size (in ml)	RayDyLyo® diameter (in mm)	Stopper type	Duration of the primary drying (in min)	Vial specific Sublimation rate (in g/vial.hour)	% variation comparing Lyo vs serum stopper (in %)
RayDyLyo®	6	20	Lyo	1530	0.117	0
RayDyLyo®	6	20	Serum	1322	0.136	-13.6
RayDyLyo®	10	20	Lyo	2454	0.122	0
RayDyLyo®	10	20	Serum	2276	0.132	-7.2

Interpretation

The 6R and 10R data are included as supporting evidence and confirm the same configuration ranking. RayDyLyo® with serum stopper remained the best RayDyLyo® option, improving primary drying by 13.6 % and 7.2% respectively for the 6R and 10R configurations. This confirms that stopper choice strongly influences performance and further supports selection of the serum-stopper configuration. It is also to be noticed that for both configurations, a similar value of vial specific sublimation is obtained respectively around 0.12g/vial.hour for the lyo stopper and 0.13 to 0.14g/vial.hour for the serum stopper. These values are considered average in the primary drying process and could constitute a decision factor when willing to switch from the conventional to the RayDyLyo® configuration without having to change the lyophilisation recipe of a specific product.

4.3. visual assessment of freeze-dried cakes

All configurations yielded cakes classified as Grade A, indicating:

- Uniform, self-supporting structure
- Adequate adherence to the vial bottom
- No collapse, meltback, puffing, or structural heterogeneity

Figure 5 presents representative images comparing cakes from the conventional configuration and RayDyLyo® configuration B. A slight "chimney-like" aspect was observed in some RayDyLyo® cakes, possibly associated with accelerated sublimation. This aesthetic variation did not affect product robustness or structural integrity.

Figure 5: Comparison of 4R vials of conventional from test run 3 (right hand side) and RayDyLyo®

From these observations, one can conclude that no major stress was put on the cake structure during the application of the conservative lyophilisation cycle.

4.4. Summary of key observations

- **Superiority of RayDyLyo® with serum stopper:** the 4R serum-stopper configuration delivered the strongest result in the study and performed essentially like naked vials.
- **Impact of the nest:** nesting did not negatively affect 4R performance and can preserve the drying advantage while supporting automation and transport.
- **Overall process impact:** RayDyLyo® combines primary drying performance with operational gains by removing the post-lyophilization crimping step and simplifying ready-to-use handling.
- **Quality:** all cakes remained Grade A across all tested configurations.
- **Practical boundary:** the benefit appears strongest at lower vial-specific sublimation rates, making this a useful specification point for client discussions.

5. Discussion

This discussion is organized around the three main messages most relevant for prospective users of RayDyLyo®. First, the 4R data demonstrate the superiority of RayDyLyo® with serum stopper. Second, the nested 4R results show that this performance benefit can be maintained in a presentation format that is attractive for automated handling and conveying. Third, these technical results translate into a broader manufacturing advantage because the RayDyLyo® concept combines drying performance with simpler aseptic operations.

The key finding is not that RayDyLyo® is universally better in every situation, but that it can significantly improve primary drying when used in the right configuration, especially in 4R vials at lower vial-specific sublimation rates. In that context, the serum-stopper configuration is clearly the leading option.

5.1. Superiority of RayDyLyo® with serum stopper

The 4R results provide the clearest demonstration of RayDyLyo® value. In the conventional reference, the vial-specific sublimation rate was 0.064 g/vial.hour. With RayDyLyo® and lyo stopper, this increased to 0.073 g/vial.hour, corresponding to a 9.6% reduction in primary drying time. With RayDyLyo® and serum stopper, the rate increased further to 0.084 g/vial.hour, corresponding to a 21.9% reduction in primary drying time.

For clients, the practical significance is simple: in the 4R range studied here, RayDyLyo® with serum stopper moves performance from a conventional 0.064 g/vial.hour to approximately 0.084 g/vial.hour, placing it essentially at the level of naked vials measured at 0.085 g/vial.hour. This makes the serum-stopper configuration the reference option for 4R when primary drying performance is a priority.

- –9.6% reduction with RayDyLyo® + lyo stopper
- –21.9% reduction with RayDyLyo® + serum stopper

The 6R and 10R results support this ranking. In both formats, the serum stopper remained the best RayDyLyo® option relative to the lyo stopper, even when the absolute outcome became less favorable in larger vials. This consistency strengthens the recommendation to prioritize the serum-stopper configuration.

5.2. Impact of the nest

The 4R nested results are strategically important because they show that the nest does not create a negative impact on primary drying. The best nested condition reached 1401 minutes and 0.086 g/vial.hour, which is essentially the same performance as naked vials and slightly better than the non-nested RayDyLyo® serum-stopper configuration. This means that the operational advantages of nesting do not need to be traded against drying performance in the 4R case studied here.

The difference between nested formats also suggests that nest design matters. Geometry influences how much glass remains exposed to gaseous conduction, while the quantity and distribution of plastic material can influence heat-transfer conditions around the vial. In practice, this means that not all nest designs should be considered equivalent, and nest optimization is a meaningful design variable for clients considering nested RayDyLyo® presentations.

At the same time, nesting brings clear process advantages: better compatibility with automation, easier transport and handling of ready-to-use vials, and elimination of the subsequent crimping step after the lyophilizer. For manufacturing teams, this operational simplification is an important part of the RayDyLyo® value proposition.

5.3. Overall impact of RayDyLyo® on manufacturing performance

The broader manufacturing message is that RayDyLyo® can deliver both technical and operational value when the application is well matched to the device. The strongest benefit appears at lower vial-specific sublimation rates, as illustrated by the 4R data around 0.084 to 0.086 g/vial.hour. From the 6R and 10R data-set, one can also distinguish a common boundary of sublimation rate at 0.12g/vial.hour for the lyo stopper and 0.13 to 0.14 g/vial.hour for the serum stopper configuration of RayDyLyo®

This makes vial-specific sublimation rate a useful reference specification for users. As a practical rule from this study, 4R applications operating in the lower-rate range are particularly promising for RayDyLyo®, especially with serum stopper and in optimized nested formats. By contrast, larger or faster-drying systems should be evaluated case by case.

When those favorable conditions are met, RayDyLyo® offers more than a primary drying gain. It also supports ready-to-use operations, simplifies handling, facilitates automation, improves conveying practicality, and removes the need for crimping after lyophilization. For clients, the attractiveness of RayDyLyo® is therefore the combination of drying performance and process simplification rather than either benefit alone.

5.4. Mechanistic interpretation

The observed performance differences can be explained in a simple way. First, the serum-stopper configuration appears to create a more favorable vapor pathway than the lyo-stopper version. Second, RayDyLyo® modifies local spacing and flow around the vial, which can support better vapor evacuation in favorable conditions. Third, the nest itself can influence heat transfer depending on its geometry and the quantity of plastic surrounding the vial, because these factors affect how much of the glass remains exposed to gaseous conduction.

- **Stopper effect:** serum stopper is the best-performing RayDyLyo® option across the tested formats.
- **Geometry effect:** RayDyLyo® can improve local vapor-flow conditions, especially in 4R.
- **Nest effect:** nest geometry and plastic quantity influence heat-transfer efficiency.
- **Rate effect:** the advantage is strongest at lower vial-specific sublimation rates.

These points are sufficient to explain why the 4R RayDyLyo® serum-stopper configuration performs so well and why nested 4R formats can remain attractive. More detailed heat-transfer work could refine this interpretation, but the current message is already clear for users.

> The RayDyLyo® device widens the lateral footprint of each vial, increasing spacing within the load. This reduces vial-to-vial shielding and enhances free vapor circulation, lowering local vapor backpressure and supporting higher sublimation rates.

For the 4R, it seems that the combination between the serum stopper and RayDyLyo® even helps recover a superior gas flow comparable to the one obtained with vials lyophilized without a stopper.

5.5. Product quality observations

Across all tested configurations:

- cakes met Grade A appearance criteria
- no collapse, meltback, puffing, or glazing was observed
- structural robustness was maintained

The slight "chimney" feature observed in RayDyLyo® cakes is consistent with accelerated sublimation at the upper surface and is commonly observed in excipient-dominant formulations dried under efficient vapor removal conditions. Importantly, it does not indicate thermal stress or structural weakness.

5.6. Industrial and Operational implications

The results have meaningful implications for pharmaceutical manufacturing:

For 4 R vials with vial-specific rates of sublimation lower than 0.122g/vial.h for the equivalent conventional configuration in the set of data presented:

1. **Potential reduction in cycle duration**
   Up to 22% decrease in primary drying time represents a substantial gain in manufacturing throughput, particularly for large-scale loads where primary drying is the dominant bottleneck.
2. **Energy and cost efficiency**
   Shorter cycles directly translate into:
   - reduced energy consumption (condensing, refrigeration, vacuum)
   - lower operating costs per batch
   - improved environmental footprint

   Use of serum stoppers in place of lyo stoppers
3. **Improved process robustness with RTU workflows**
   RayDyLyo® enables:
   - removal of the post-freeze-drying crimping step
   - reduction of Grade A interventions
   - improved compliance with Annex 1 expectations
   - compatibility with automated, robotic or isolator-based manufacturing

The finding that RayDyLyo® does not compromise and may even enhance freeze-drying efficiency supports its use in fully integrated RTU aseptic workflows.

5.7. Industrial and Operational implications

To confirm and expand upon these findings, the following studies are recommended:

1. Measure Kv (heat transfer) for each configuration to quantify mechanistic drivers.
2. Perform thermal mapping using multiple vials and different shelf positions.
3. Conduct multiformulation trials, including protein-based products sensitive to thermal stress.
4. Include analytical characterization (residual moisture, DSC, SEM) to assess product quality more comprehensively.
5. Repeat runs to establish statistical variability and cycle reproducibility.

6. Conclusion

This white paper shows that the strongest RayDyLyo® result was obtained in 4R vials and that the preferred configuration is RayDyLyo® with serum stopper. In 4R, this configuration reduced primary drying time by 21.9% versus the conventional reference and delivered a vial-specific sublimation rate of 0.084 g/vial.hour, essentially equivalent to the naked-vial reference at 0.085 g/vial.hour. All cakes remained Grade A.

The 6R and 10R data support the same hierarchy of configurations: the serum stopper consistently performs better than the lyo stopper within the RayDyLyo® platform. The data also suggest that the benefit is strongest at lower vial-specific sublimation rates, making this a practical reference point for selecting suitable applications.

The 4R nested results are equally important because they show that nesting does not create a drying penalty and can remain compatible with high performance. This supports the use of nested presentations for automation, easier and safer conveying of ready-to-use vials, and simplified operations.

Overall, RayDyLyo® should be viewed as a manufacturing-performance solution as much as a closure solution. In favorable 4R conditions, it combines improved primary drying, no visible quality penalty, compatibility with nesting, easier automated handling, and elimination of post-lyophilization crimping.

For clients evaluating RayDyLyo®, the key takeaway is straightforward: if the target application resembles the 4R drying regime studied here, RayDyLyo® with serum stopper is the lead configuration to consider.

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8. Credits

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