# Assessing the particle concentration of mRNA-LNP using Corning® Videodrop

## A new metric for Lipid Nanoparticles (LNP) manufacturing, optimization and standardization

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## Application Note

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### Introduction

Corning Videodrop is an innovative nanoscale imaging technology. Based on the principle of interferometry, Corning Videodrop makes it possible to measure the size and concentration of nanoparticles.

- In real-time (40 s)
- In a single drop (7 µL)
- Between 80 to 500 nm
- Within a concentration range of $10^8$ to $10^{10}$ part/mL
- Without labeling

Here, we propose to use Corning Videodrop for the analysis of mRNA-LNP and highlight the interest of measuring the particle concentration of mRNA-LNP (Figure 1).

The current analytical strategies employed for mRNA-LNP characterization lie primarily on size, polydispersity, and zeta-potential measurements. However, particle concentration, evaluated through a single particle measurement technique, is an important parameter to monitor for several reasons (Figure 2).

- Quality control tests
- Stability assessment
- Standardization for comparative studies

When developing new formulations, manufacturing processes, or different storage conditions, quantifying the number of particles enables efficient comparison studies. By comparing particle numbers under different conditions, researchers can assess the impact of the process or composition on transfection activity.

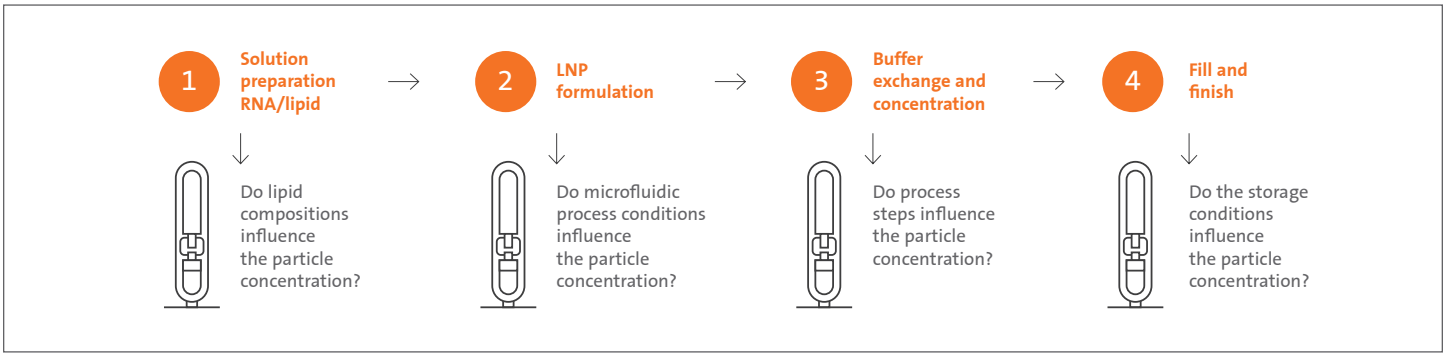


**Figure 1.** Importance of LNP particle concentration.

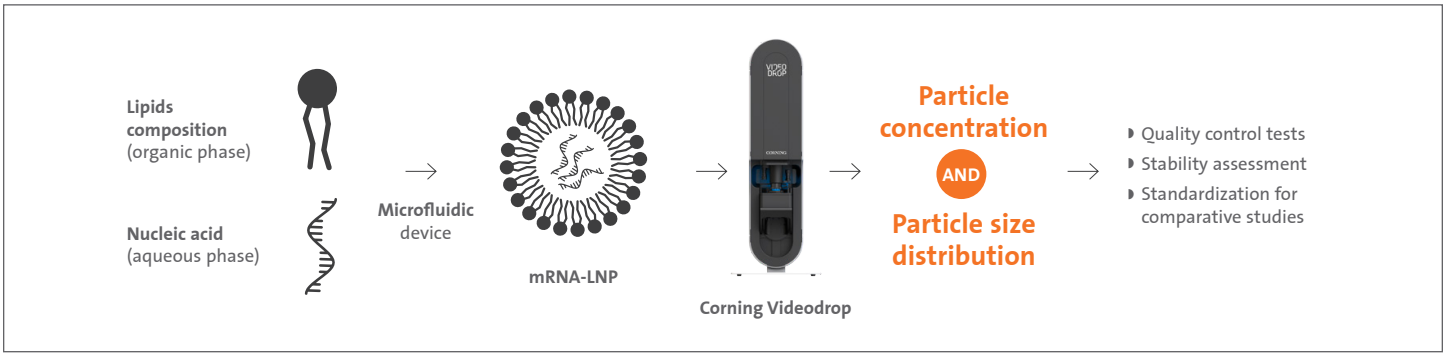


**Figure 2.** Corning Videodrop applications.

## Results

### 1. Solution Preparation RNA/Lipid – Lipid Composition Optimization

Two LNPs with different lipid compositions were produced using the same process. Particle concentration was not affected by the lipid composition (Figure 3); however, Lipid Composition 1 exhibits higher activity compared to Lipid Composition 2.

Despite having approximately the same number of particles, Lipid Composition 1 was more efficient compared to Lipid Composition 2.

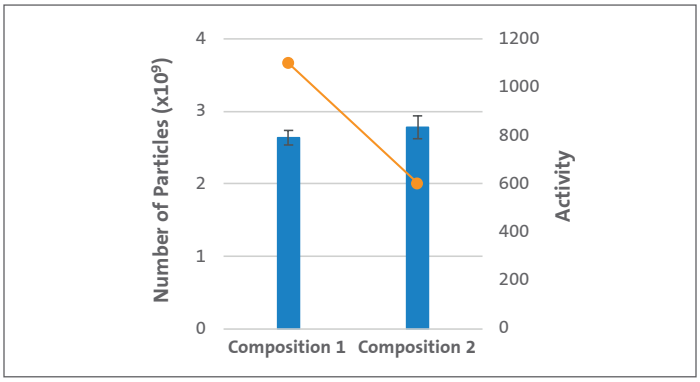


**Figure 3.** Comparision of the two LNPs with different lipid compositions.

### 2. LNP Formulation – Mixing Speed Optimization

We compared LNPs having the same composition but prepared with different mixing speeds (flow rates) on the microfluidic device.

The mixing speed step had a significant influence on the concentration of the generated particles (Figure 4).

The activity was directly related to the number of particles.

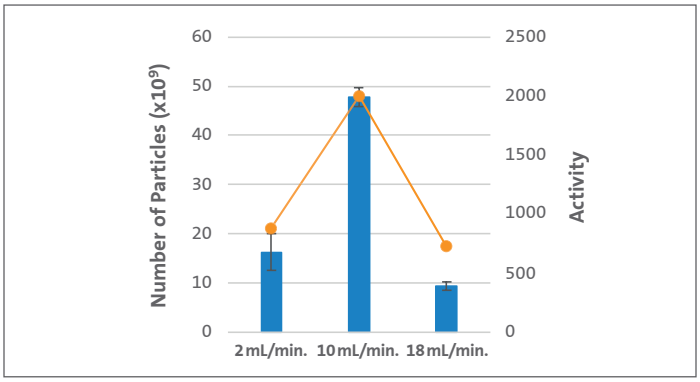


**Figure 4.** Influence of the mixing speed on the concentration of the generated particles.

### 3. Buffer Exchange and Concentration – Buffer Exchange Optimization

Buffer exchange and concentration steps are crucial and require optimization to improve the yield.

This experiment examined the influence of incorporating a buffer exchange step.

The buffer exchange step resulted in a 75% reduction in the number of particles (Figure 5).

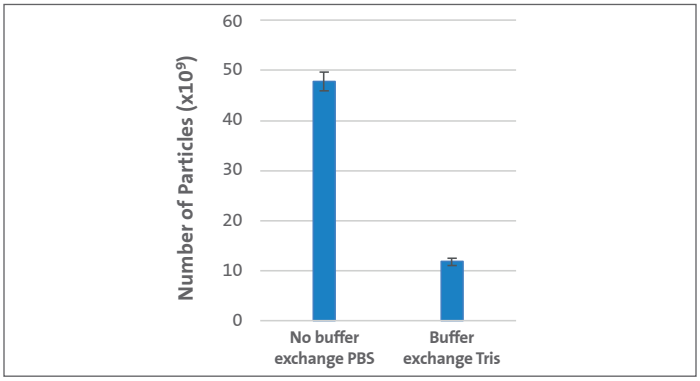


**Figure 5.** Influence of incorporating a buffer exchange step.

### 4. Fill and Finish – Storage Optimization

To ensure product quality, it is essential to optimize storage conditions.

We tested the same product stored at +4°C or -20°C.

The results indicated that the storage at -20°C led to a decrease in the number of particles as well as a loss in activity (Figure 6).

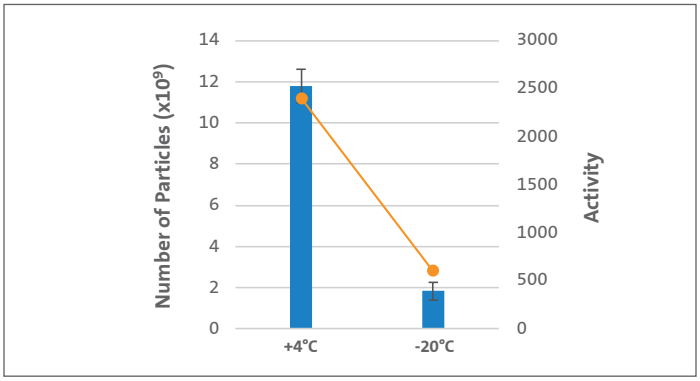


**Figure 6.** Influence of the storage temperature on the number of particles.

## Conclusions

- Corning® Videodrop is a ready-to-use tool for measuring the particle concentration of LNPs in a single drop.
- Corning Videodrop enables better control of the production process by quickly and easily measuring the concentration.
- Corning Videodrop is the ideal tool to complete the analytical strategy to assess LNP quality.



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