

Lyophilization of RNA-LNPs in 96-well plate – A small-scale, high-throughput approach for excipient screening of lyophilized LNPs



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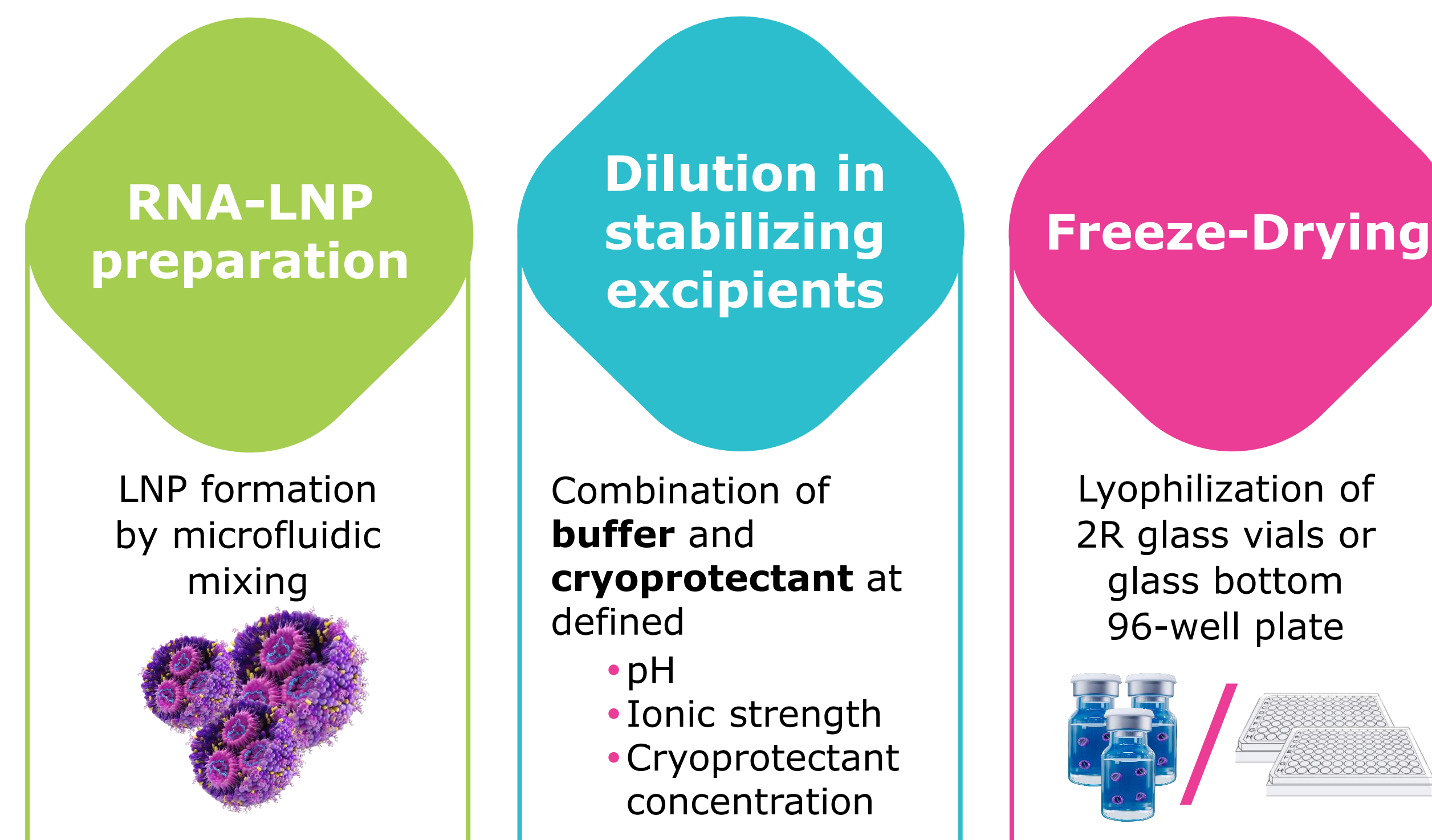
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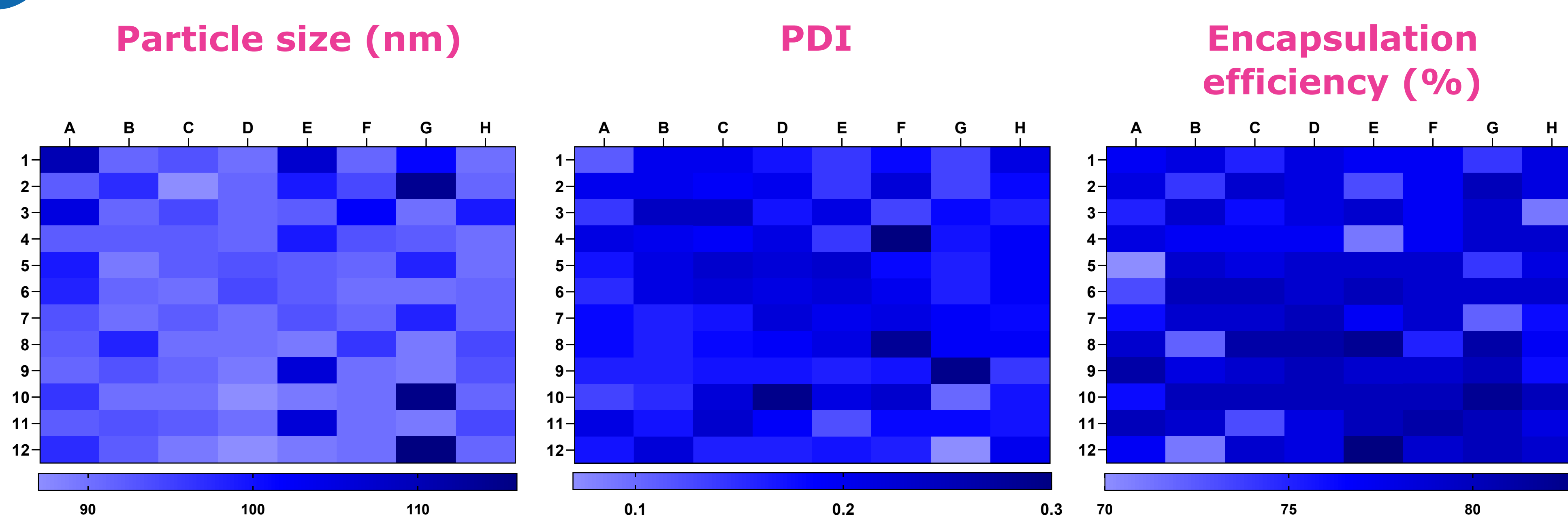
objective

- Lyophilization** is a widely adopted strategy in pharmaceutical industry to **stabilize sensitive formulations**, such as lipid nanoparticles (LNPs)
- Challenge:** Developing robust lyophilization is **capital-** and **time-intensive**, with stabilizing excipients driving critical quality attributes (CQAs)
- High-throughput (HTS) lyophilization in 96-well plates** enables rapid, small-scale excipient screening for LNPs
- Outcome:** Faster identification of robust, scalable lyophilization formulations

workflow

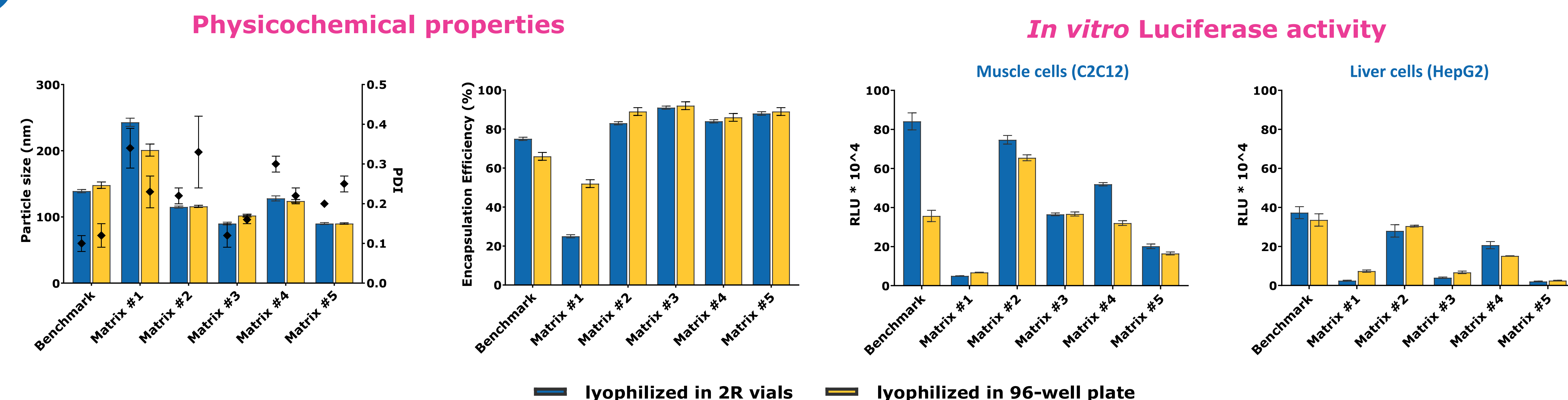


reproducibility



- ✓ High reproducibility across the plate with average
Particle size ~90 nm
PDI < 0.3
EE (%) > 78 %
- ✓ Deviation < 10 %
- ✗ Minor edge effect at corner wells with increased particle size and decreased EE (%)

comparability



- Lyophilized LNPs in glass bottom **96-well plate** and **2R glass vials**
 - ✓ Show high comparable physicochemical properties and *in vitro* performance in different cell lines
 - ✓ Allows screening of multiple buffer-cryoprotectant combination (matrix) within one lyophilization run
- Different types of matrices could enhance *in vitro* performance and contribute to final product attributes

summary

- ✓ **High-throughput** – suitable and representative strategy to accelerate the development of lyophilized LNP in aspect of time and effort
→ simultaneous **screening of multiple formulation conditions** and/or stabilizing excipients possible
- ✓ **Small-scale** – minimizes the amount of required material, making it particularly advantageous during early-stage formulation development
- ✓ **Cost-effectiveness** – reduces expenses compared to conventional lyophilization with 2R glass vials
- ✗ **Possible edge effects** – different temperature and drying conditions compared to centered wells

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