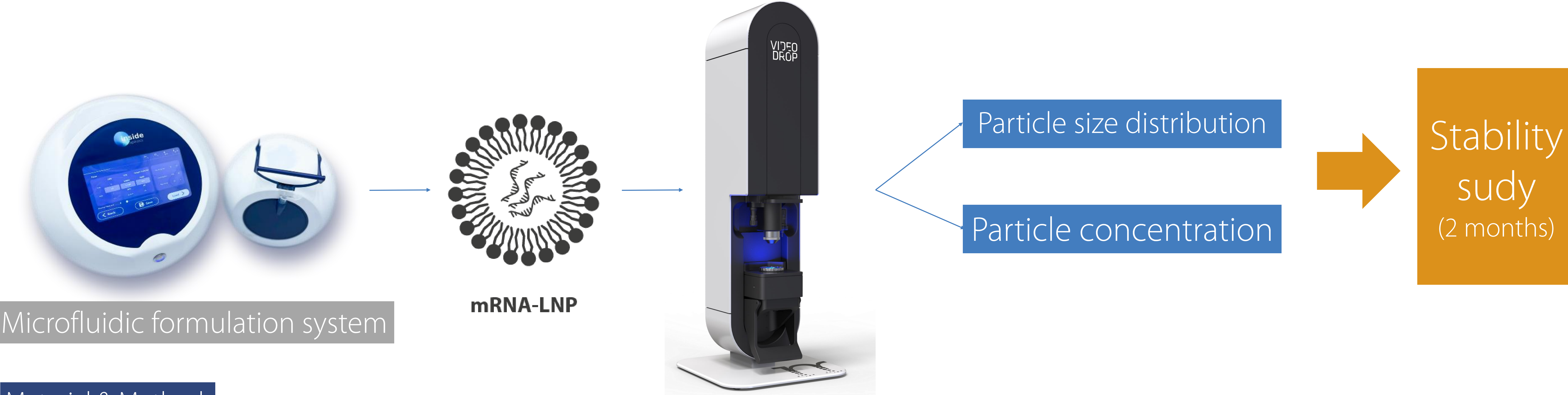


Lipid nanoparticle (LNP) therapy development is a challenge. Using the proper tools and metrics is a key success factor. The solution presented here, combining VIDEODROP (Myriade) and TAMARA (Inside Tx), offers a rapid and comprehensive screening and assessment capability for LNP formulation and stability studies. This study leverages VIDEODROP, a fast & user-friendly nanoparticle analysis instrument, to quantify LNP sample size distribution and concentration within a single droplet. The LNPs were synthesized using TAMARA, an easy-to-use microfluidics nanoparticle synthesis platform. This platform enabled the production of numerous LNP samples with varying key formulation parameters, including microfluidics characteristics (total flow rate [TFR] and flow rate ratio [FRR]) and formulation components (presence or absence of a PEGylated lipid).



Material & Method:

Screening of different formulation conditions using Tamara microfluidic system

Parameter	Total Flow Rate (TFR)	Flow Rate Ratio (FRR)	PEG
# of values	3	2	2
Values	1; 2; 5 mL/min	3/1 , 6/1	With / Without

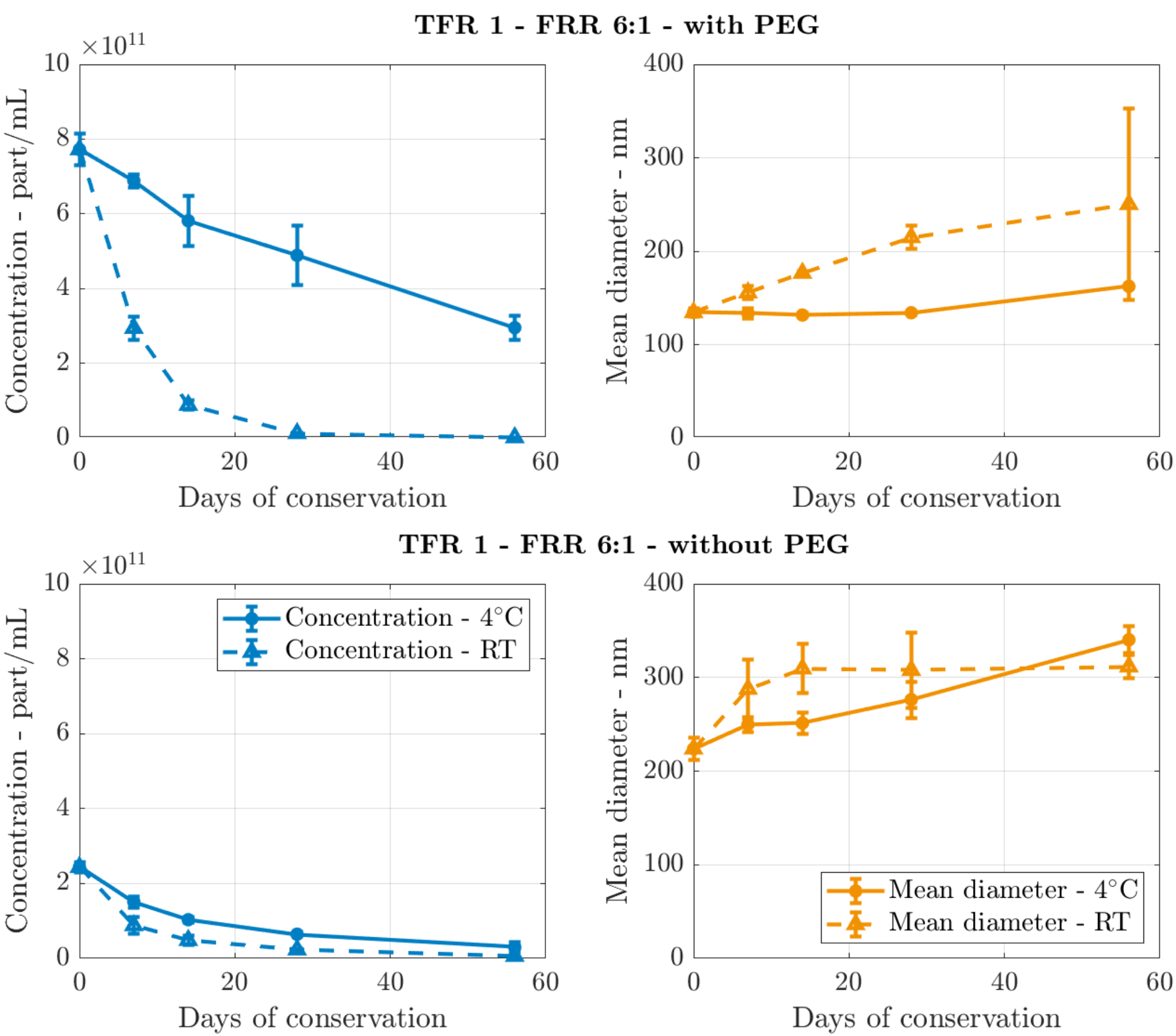
Stability study

Parameter	Storage temperature	Time points
# of values	2	5
Values	+4°C ; RT	D0; D7; D14; D28; D56

Results :

1 Focus on 1 set of condition:

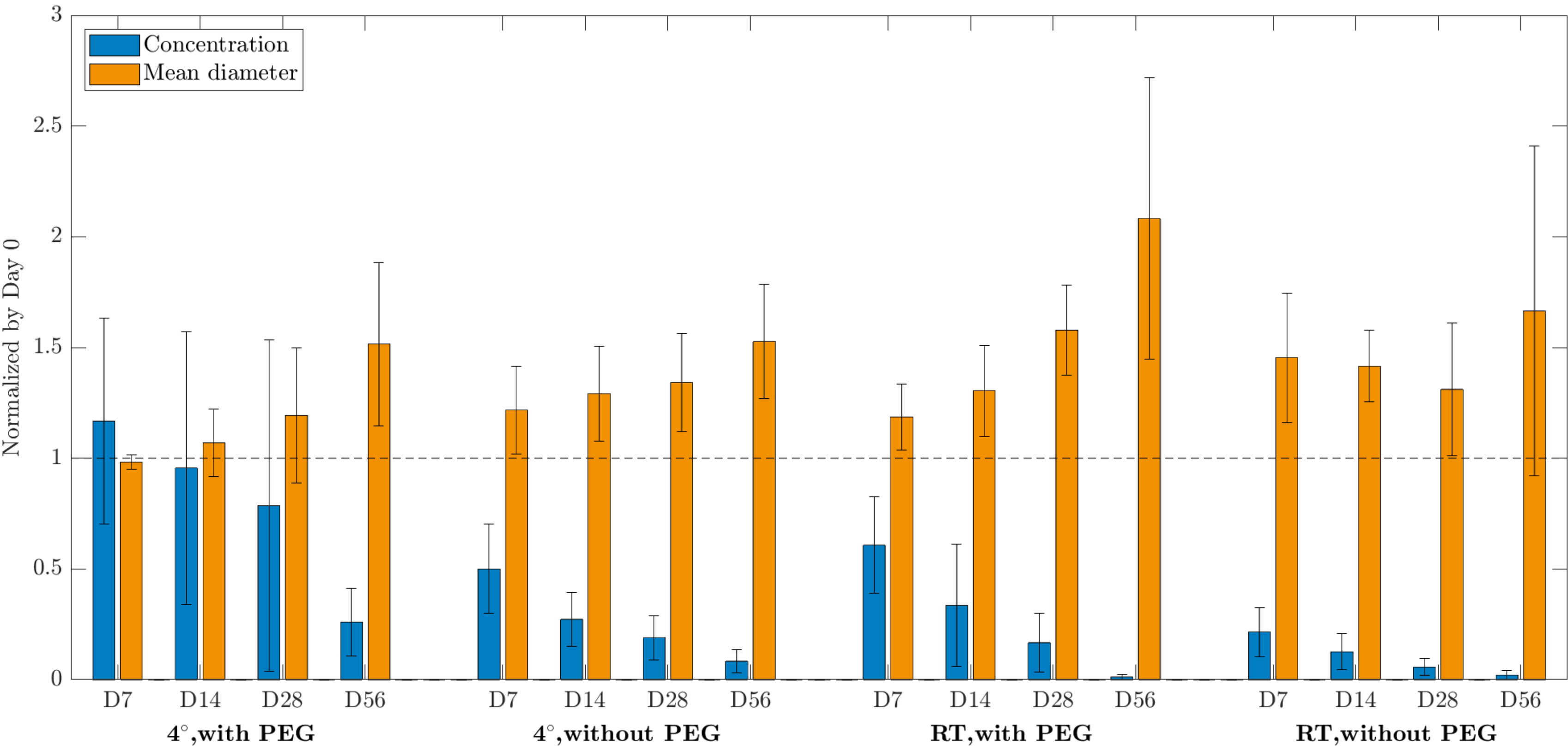
This figure illustrates the size and concentration evolution of several specific formulation conditions over time.



- Mean diameter increases & Concentration decreases over time.
- Slower phenomenon at +4°C & with PEG.

2 Average of all set of conditions:

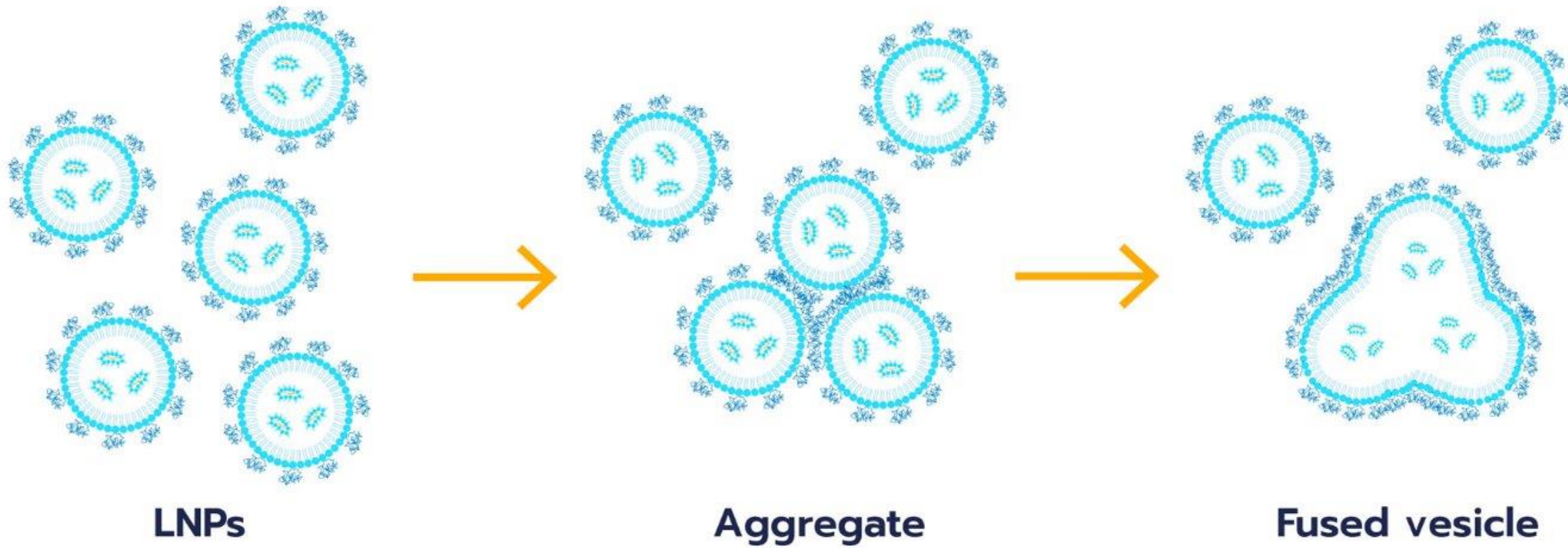
In this figure, we summarize the stability study results over all conditions (TFR and FRR) and analyse the impact of the temperature and presence of PEG on the particle size and concentration .



- Confirmation of previous observations.
- The condition enabling the best stability is the presence of PEG and storage at 4°C.

3 Destabilisation phenomenon:

From the results we obtain, the following destabilisation phenomenon might be the explanation of the results we observe : LNPs first aggregate before fusing together. It matches experimental observations of progressive size increase and concentration decrease.



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Videodrop, by measuring size and particle concentration, evidence how microfluidics parameters, composition, and dialysis impact both size distribution and concentration, allowing for the fine-tuning of formulation features. The stability study emphasize the role of PEG to stabilize the formulations over time. LNP samples containing PEG and stored at 4°C keep their size and concentration constant over a month. Without PEG and at RT sizes quickly increase and concentrations drop.

The VIDEODROP and TAMARA are the right set of tools to enable fast, straightforward and comprehensive LNP formulation screening and stability optimization.