IN-USE STABILITY OF COMIRNATY AND SPIKEVAX CLINICAL SOLUTIONS: PFIZER-BIONTECH AND MODERNA COVID-19 VACCINES. A COMPARATIVE STUDY FROM A HOSPITAL PHARMACY PERSPECTIVE

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BACKGROUND AND IMPORTANCE

- COVID-19 outbreaks in the late 2019, expanding very rapidly globally, being categorised as pandemic in March 2020 by WHO. Pfizer-BioNTech and Moderna launched their COVID-19 vaccines, namely Comirnaty and Spikevax by the late 2020 and early 2021 respectively, having demonstrated efficacy and safety.
- One of the major issues with these vaccines is the instability of the mRNA molecule embedded in lipid nanoparticles (LNPs) [**1**]. In addition, scarce in-use stability data is available in the public domain, which will be of interest for health professionals.
- Dynamic Light Scattering is a powerful and sensitive technique to assess the physical properties of the mRNA-LNP complex, enabling the detection of degraded products.

AIMS

This study is aimed at assessing and comparing the in-use stability of Comirnaty and Spikevax clinical solutions by characterizing the particulate profile using Dynamic Light Scattering (DLS).

Characterize and compare the particle profiles of Comirnaty and Spikevax vaccines by DLS.

Assess and compare the robustness of Comirnaty and Spikevax dispersions in relation to their handling.

MATERIALS AND METHODS

1) Samples preparation

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Summary of Product Characteristics

Comirnaty

Purple tape vials
0.45 mL of concentrate for dispersion for injection, dilution in 1.8 mL of NaCl, 6 doses of 0.3 mL

Unexpired | Expired

Spikevax

Red tape vials
5 mL of a ready to administer concentrate for dispersion for injection, 10 singles doses of 0.5 mL.

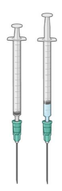
Unexpired | Expired

2) Stress testing

A) Light irradiation (250 W/m2), 24 h

B) Vigorous manual shaking (10 s)

C) Aspiration/release cycles, 1x and 3x



D) Vortex vibration, 2400 rpm (10 s)

3) Analysis

Zetasizer Nano ZS-90

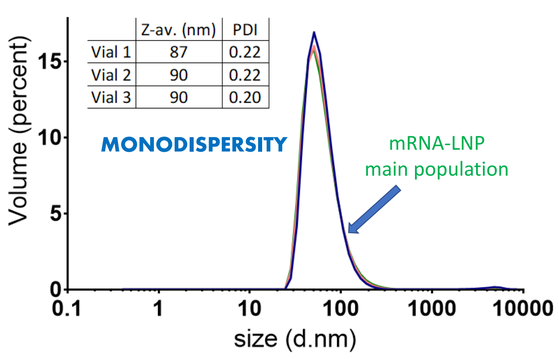
Statistical analysis

Prism

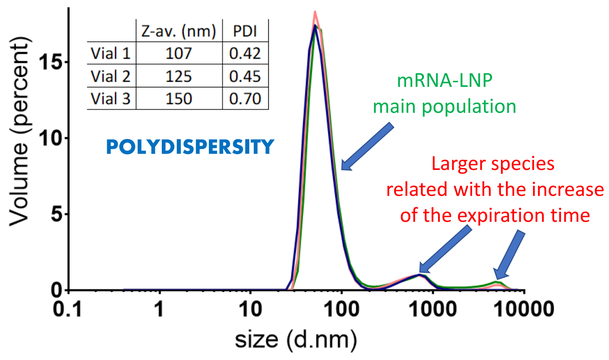
RESULTS

Characterization

Unexpired Comirnaty vials

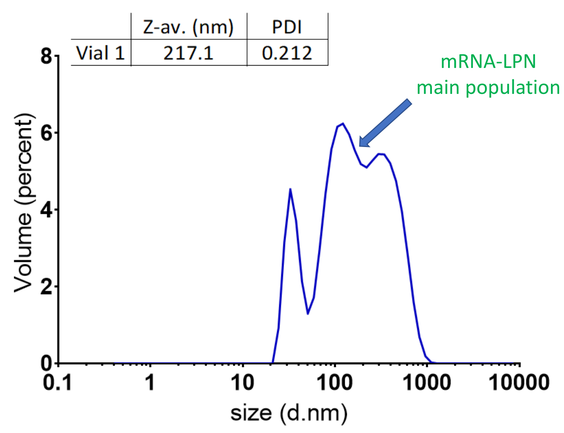


Expired Comirnaty vials

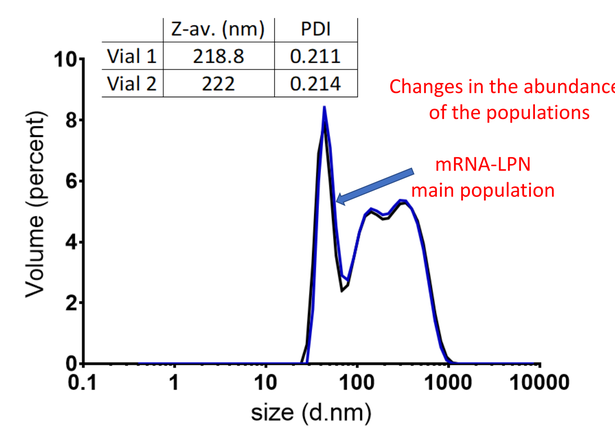


- Comirnaty **unexpired** samples were characterised by a main population of mRNA-LNPs with average D_h of 60-65 nm, representing over 99 % of the total volume, indicating monodispersity. In Comirnaty **expired** samples, this main population decreased up to 90 %, proportional to expiry dates: vial 1: 94 % (1 month exp), vial 2: 92 % (2 months exp) and vial 3: 90 % (4 months exp), two new populations were observed and in consequence, Z-average and PDI increased significantly and progressively; therefore, **increase in the expiration time led to increased particle size and content of larger species detected by DLS** (in accordance to ref [2])**.**

Unexpired Spikevax vials



Expired Spikevax vials



- **Spikevax DLS results were more complex to interpret than Comirnaty**. Spikevax unexpired samples were characterised by 3 unresolved size populations from 30 to 1000 nm (the main one with D_h 100-200 nm represented a 50 % of the total volume); despite this, polydispersity was not clearly indicated by PDI values. In the expired samples, changes in the volume percents of these three size populations occurred (the main was the one with D_h of 40 nm), while the size range (30 to 1000 nm) was kept. Despite these modifications, neither Z-average nor PDI increased significantly after expiration, **therefore expiration time did not lead to increases in the particle size and content of larger species detected by DLS .**

Stress testing

TABLE 1

Vaccines \ Parameters	Stress test	Z-average (nm)	PDI
Pfizer-BioNTech (Comirnaty)	Control 1 **(Exp)**	146.6 ± 3.3	0.69 ± 0.04
	Artificial light 24 h	146.3 ± 2.3	0.70 ± 0.04
	Control 2 **(Exp)**	148.7 ± 4.0	0.70 ± 0.04
	Manual shaking	173.7 ± 19.5	0.69 ± 0.13
	Vortex vibration	165.0 ± 7.2	0.74 ± 0.04
	Control 3 **(Exp)**	147.1 ± 0.6	0.71 ± 0.03
	Syringe injection (1x)	149.1 ± 3.1	0.73 ± 0.01
	Syringe injection (3x)	156.2 ± 6.2	0.66 ± 0.01
	Control 4 **(Unexpired)**	88.0 ± 1.3	0.23 ± 0.01
	Manual shaking	**115.7 ± 7.5***	**0.38 ± 0.02***
	Vortex vibration	95.6 ± 1.2	0.26 ± 0.01
Moderna (Spikevax)	Control 1 **(Exp)**	219.6 ± 2.1	0.22 ± 0.01
	Natural light 24 h	214.7 ± 2.1	0.22 ± 0.01
	Control 2 **(Exp)**	221.0 ± 3.6	0.21 ± 0.01
	Manual shaking	222.1 ± 2.7	0.23 ± 0.01
	Vortex vibration	220.0 ± 4.4	0.22 ± 0.01
	Control 3 **(Exp)**	219.6 ± 2.1	0.22 ± 0.01
	Syringe injection (1x)	219.5 ± 2.0	0.22 ± 0.01
	Syringe injection (3x)	218.8 ± 2.6	0.22 ± 0.01
	Control 4 **(Unexpired)**	218.3 ± 1.3	0.22 ± 0.00
	Manual shaking	221.5 ± 2.7	0.23 ± 0.01
	Vortex vibration	216.1 ± 2.3	0.21 ± 0.01

- **Results:** Table 1 includes the Z-average and PDI values (mean ± SD from 3 independent replicates) of unexpired and expired Comirnaty and Spikevax samples after stress testing. The only statistically significant differences were found in unexpired Comirnaty samples after applying vigorous manual shaking. In addition, these parameters were notoriously different in expired Comirnaty samples in comparison with the unexpired ones. On the other hand, these parameters were not affected in Spikevax samples regardless of stress testing and expiration.

CONCLUDING REMARKS

- Comirnaty and Spikevax dispersions were characterized by remarkable different particle profiles; being the average particles size smaller in Comirnaty than in Spikevax samples.
- The particle profiles in unexpired samples were different to expired samples: in Comirnaty, expiration time led to increased particle size and content of larger species while in Spikevax, particles ranged between 30-1000 nm, finding modifications in the relative abundances of each population.
- The particle profile in Comirnaty dispersions seemed to be particularly sensitive to mechanical stresses, while accelerated light exposition had no effect on neither of the vaccines dispersions.

REFERENCES

[**1**] Schoenmaker, L., Witzigmann, D., Kulkarni, J. A., Verbeke, R., Kersten, G., Jiskoot, W., & Crommelin, D. J. A. (2021). mRNA-lipid nanoparticle COVID-19 vaccines: Structure and stability. International Journal of Pharmaceutics, 601, 120586. https://doi.org/10.1016/j.ijpharm.2021.120586

[**2**] Thaller, A., Schmauder, L., Frieß, W., Winter, G., Menzen, T., Hawe, A., Richter, K. (2023). SV-AUC as a stability-indicating method for the characterization of mRNA-LNPs. European Journal of Pharmaceutics and Biopharmaceutics 182, 152–156. https://doi.org/10.1016/j.ejpb.2022.11.014

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