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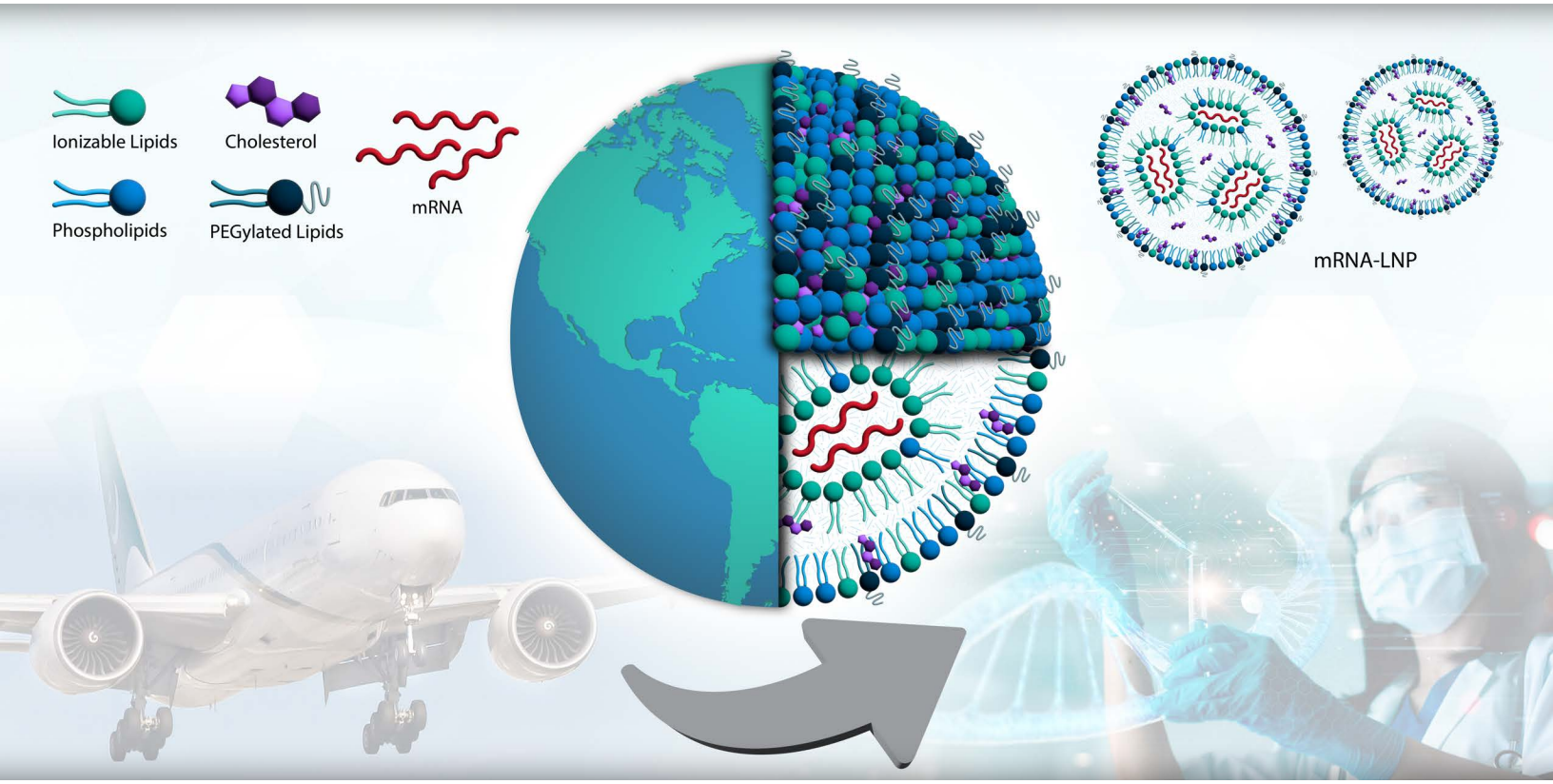
Concerned about mRNA - LNP integrity during international shipping?



Several batches of mRNA-LNP samples, shipped by CATUG (CDMO in China), were subjected to Quality Control-style testing performed at the receiving site (Crystal Bio, New Jersey, USA) to address the concerns surrounding mRNA -LNP integrity during international shipping[1,2].

In this article, data from key tests for size with distribution, encapsulation, and purity on mRNA-LNP, were compared between the 2 sites.

Read more

mRNA - LNP Integrity During International Shipping

Several batches of mRNA-LNP samples, shipped by CATUG (CDMO in China), were subjected to Quality Control-style testing performed at the receiving site (Crystal Bio, New Jersey, USA) to address the concerns surrounding mRNA -LNP integrity during international shipping[1,2].

Data from key tests for size with distribution, encapsulation, and purity on mRNA-LNP, were compared between the 2 sites, as:

Table 1

Batch	Shipping site			
	Purity (%)	Encapsulation (%)	Size with distribution	
			Z (nM)	PDI
A	81.9	92.4	75.3	0.11
B	82.6	95.8	68.7	0.06
C	82.4	96.5	68.1	0.1

Batch	Receiving site			
	Purity (%)	Encapsulation (%)	Size with distribution	
			Z (nM)	PDI
A	81.7	91.6	71.6	0.078
B	81.5	91.0	76.5	0.097
C	81.7	93.5	74.1	0.099

Samples spent ~3 days in transit and were analyzed immediately after they were de-frozen.

There is no significant difference in data between the shipping and receiving sites as measured by mRNA purity, mRNA-LNP encapsulation, and size with distribution (average size as Z with polydispersity index as PDI), as shown in Table 1.

In addition, after being de-frozen, these samples were maintained without cold control and were left at room temperature for 2 days, before further testing for size with distribution measurement. These tests showed very similar results (data not shown).

Further, one vial from batch (B), shipped at different time (after several transit stops), was tested again, as:

Table 2

Batch	Shipping site			
	Purity (%)	Encapsulation (%)	Size with distribution	
			Z (nM)	PDI
B	82.6	95.8	68.7	0.06

Batch	Receiving site			
	Purity (%)	Encapsulation (%)	Size with distribution	
			Z (nM)	PDI
B	81.7	88.03	118	0.12

In this batch (after several transit stops and with sufficient dry ice in the package), the size estimation (with distribution measurement) showed increase but no difference in purity with slight decrease in encapsulation at the receiving site, as shown in Table 2. While the purity of mRNA is maintained, we do not know whether the increase in size may influence mRNA-LNP bioactivity (eg, protein expression). Nevertheless, for the sake of caution, this batch or vial may be eliminated after screening by QC-style testing at the receiving site.

Test Methods:

- mRNA purity - by ion-paring reverse-phase liquid chromatography (IP- RPLC).
- Encapsulation - by a fluorescence-based Ribogreen assay.
- Size - by Dynamic Light Scattering (DLS) for average size as Z-average.
- Distribution – by DLS to measure polydispersity index (PDI).

Are you concerned about mRNA - LNP integrity during international shipping?

It should not be a major concern, and scientists can be particularly reassured by further QC-style testing at the receiving site. On further examination, the cold temperature control did not seem to affect the integrity of mRNA (for instance, within a day or two with sufficient / insufficient dry ice in the package) while a package with more transit stops (with possibly higher probability of shaking) may affect the size with distribution but not purity (with small change in encapsulation).

Capabilities at Crystal Bio

Crystal Bio is a leading Contract Research Organization (CRO) specializing in comprehensive analytical services for biotherapeutics. Our expertise covers a wide range of modalities, including mRNA-LNP therapeutics with our strategic partner CATUG ; Antibody Drug Conjugates (ADCs); Monoclonal Antibodies; and Fusion Protein. With a robust bio-analytical toolkit comprising High-resolution LC-MS, IPRP-LC,RPLC, LC-ELSD, LC-CAD, CE, IEF, qPCR, ELISA, sterility, bioburden and cell-based bioassays etc. Our capabilities also extend to method development and analytical characterization of biotherapeutics. This holistic approach ensures compliance with stringent regulatory requirements outlined in the CMC section, making us a valuable partner for pre-IND, Phase I, and subsequent submissions.

References:

1. Muramatsu H, Lam K, Bajusz C, Laczkó D, Karikó K,Schreiner P, Martin A, Lutwyche P, Heyes, Pardi N. Lyophilization provides long-term stability for a lipid nanoparticle-formulated, nucleoside-modified mRNA vaccine. Molecular Therapy, 2022, 30 (5), 1941-1951.
2. Reinhart AG, Osterwald A, Ringler P, Leiser Y, Lauer ME, Martin RE, Ullmer C, Schumacher F, Korm C, Keller M. Investigations into mRNA Lipid Nanoparticles Shelf-Life Stability under Nonfrozen Conditions. Molecular Pharmaceutics, 2023, 20 (12).