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Improved Ad26 vaccine stability by mitigating interaction of viral particles with glass surfaces

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IMPROVED Ad26 VACCINE STABILITY BY MITIGATING INTERACTION OF VIRAL PARTICLES WITH GLASS SURFACES

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Long term vaccine stability at refrigerated temperatures (2-8°C and ambient) is critical to ensure a global reach of the vaccine using a standardized supply chain. During Ad26 clinical vaccine development, some instability at 2-8°C was observed which triggered a root cause investigation. There was a risk that the target shelf life of at least 2 years at 2-8°C would not be met.

The root cause was identified as adsorption of viral particles (vp's) to the glass surface. This phenomenon is in particular observed upon inversion of the vial at 2-8°C due to the additional loss of vp's to unexposed glass surface. Various innovative analytical tools were applied including spectroscopic kinetic monitoring of the loss of the vp's directly inside the 2R glass vials. This was enabled by creating custom 3D printed accessories to fit the equipment. Models were created that allowed further predictions on the amount of vp's adsorbed, dependent on volume, titer and vial type. Additional orthogonal analytical methods were applied to confirm the results, such as visualizing adsorbed material by dyes (staining) on the glass walls (Figure 1) as well as determining the vp content using VPqPCR and CZE.

A dual mitigation was implemented for the Ad26-based vaccines to avoid further loss of vp's during shelf life of the vaccines to the glass surface and to enable a sufficient long shelf life at refrigerated conditions.

i) For single dose vaccines (eg Ad26.RSV.preF) the primary container was changed to siliconized glass vials. Large scale manufactured drug product vaccines showed an improved stability profile at 2-8°C and confirmed that the proposed mitigations were successful. The stability is now in line with reaching a target shelf life of at least 24 months.
ii) For multi dose vaccines, (eg Ad26.COV2.S 5-dose vaccine) an overage was applied to compensate for the process loss in combination with maximizing the fill volume for the 2R glass vial. As such, upon inversion, any additional loss of vp's to glass surface was negligible as the vials were filled to the max, allowing administration of 5 doses of 0.5mL from every vial. This was critical as the standard type 1 glass vials were available in large amounts during the onset of the covid pandemic.

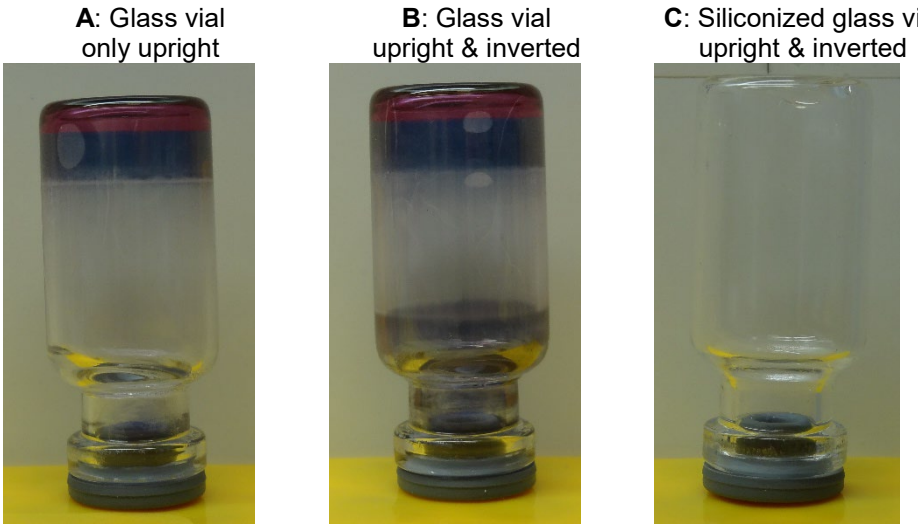

Figure 1 – Visualization of adsorption of viral particles to glass surface. No adsorption visible with siliconized glass vials.