INX100441648: 6th Dose Evaluation of Poonglim Low Dead Space Prototype Safety Needle and Syringe

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1. INTRODUCTION

Prototype low dead-space (LDS) syringes with companion safety needle developed by Poonglim was evaluated to determine if they can deliver 6 doses of BNT162b COVID-19 vaccine drug product and if they meet previously determined dead-space requirements to ensure consistent removal of 6 doses. This report documents the assessment of the Poonglim LDS components to effectively remove and administer 6 doses of vaccine from a single vial.

2. BACKGROUND

The BNT162b drug product is manufactured at a nominal fill volume of 0.45 mL and a concentration of 0.5 mg/mL mRNA-LNP for a total content of 225 µg. Upon thaw and dilution with 1.8 mL saline, according to the instructions for use, the resultant volume is 2.25 mL at 0.1 mg/mL. At this concentration, the dose of 30 µg is delivered to the patient's intra-muscular tissue by an injection of 0.3 mL.

Standard syringes and needles, when correctly assembled, may have a range of liquid hold-up volumes resulting in approximately 0.1 mL (100 µL) loss within the syringe / needle combination (Kume, 2012). This 100 µL hold-up volume is accounted for in the design of the product when utilizing standard needles and syringes. See Table 1 for a description.

In contrast, the use of low dead-space syringes and needles may reduce this hold-up volume to enable a more efficient use of liquid (Keston, 2017). Assuming a hold-up volume of 0.035 mL (35 µL), one can calculate that 6 doses of 0.3 mL each can be administered from the same vial that would enable 5 doses with standard syringes and needles. See Table 1 for a description. In the interest of reducing wasted doses and maximizing the use of BNT162b drug product for the prevention of COVID-19 infection, the use of LDS components may enable a greater number of doses to be administered.

Table 1. Impact to Vial Volumes from Standard vs Low Dead-Space Components

Standard Syringe and Needle			Low Dead-Space Syringe and Needles		
Step (5 dose)	**Required Volume**	**Total Volume**	**Step (6 dose)**	**Required Volume**	**Total Volume**
5 doses	5 x 0.3 mL per dose	1.5 mL	6 doses	6 x 0.3 mL per dose	1.8 mL
Dosing syringe overage	5 x 0.1 mL per syringe	0.5 mL	Dosing syringe overage	6 x 0.035 mL per syringe	0.21 mL
Non-extractable volume	0.15 mL	0.15 mL	Non-extractable volume	0.15 mL	0.15 mL
Additional Volume to simplify instructions	0.1 mL	0.1 mL	Additional Volume to simplify instructions	0.09 mL	0.09 mL
Total Volume		2.25 mL	Total Volume		2.25 mL

In Table 1, the left three columns describe the calculations for a standard needle and syringe combination. 3 doses at 0.3 mL each will require 1.5 mL total volume. A hold-up volume of 0.1 mL is assumed for each dosing syringe for a total of 0.5 mL. 0.15 mL remains in the neck of the vial and cannot be removed. Finally, 0.1 mL is included as result of simplifying dilution and dose volumes (i.e. dosing according to 0.1 mL graduations on a dosing syringe). The sum is 2.25 mL. The right three columns demonstrate the same calculations using low dead-space components. In this case, 6 doses at 0.3 mL are delivered. The hold-up volume of 0.035 mL is included for a total loss of 0.21 mL. The vial hold up and additional volume remain comparable. Again, the sum is 2.25 mL.

3. SUPPORTIVE DATA

Low dead-space prototype components, a 1 mL LDS luer lock syringe, and 25G 1" safety needle, were procured from Poonglim. Needle-syringe pairings were assessed for hold-up volumes and assessed for the ability to deliver 6 doses of vaccine from representative vials.

Vials were prepared in a development laboratory filing drug product to a target volume of 0.416 mL, which represents the lower end of the normal fill weight range during manufacture. This afforded a more robust challenge to the components ability to deliver 6 doses. The vials were then diluted with 1.8 mL 0.9% sodium chloride injection.

Tables 2 and 3 include data from the evaluation conducted to assess feasibility of the combined Poonglim components to deliver 6 doses from a low-fill drug product vial. After the vial was diluted, six withdrawals were performed using a new, pre-weighed needle and syringe for each withdrawal. On the 6th withdrawal, all remaining extractable content of the vial was withdrawn. The six withdrawals were then ejected, pooled, the cumulative weight recorded, then converted to volume using the density of the diluted vaccine (1.0122 g/mL). The total volume delivered must be greater than or equal to 1.8 mL (6 x 0.3 mL doses). Additionally, the average hold up volume for each syringe plus needle combination was calculated by reweighing the needle/syringe after the volume was ejected. If the average hold up volume for the six

determinations was ≤35 µL, the combination was determined to be suitable to ensure six doses may be delivered.

Table 2. Weights of 6 doses extracted and delivered from Poonglim prototype LDS syringes

	Dose 1 (g)	+Dose 2 (g)	+Dose 3 (g)	+Dose 4 (g)	+Dose 5 (g)	+Dose 6 (g)	Total Delivered (mL)
Pooled Dosing Solution	0.294	0.590	0.886	1.182	1.481	2.085	2.060

Table 3. Hold up volume determination of Poonglim prototype LDS syringes

	weight empty (g)	weight after dose expelled (g)	Hold up (g)	Average Hold up (g)	Hold up (mL)	Average Hold up (mL)
Syringe #1	5.223	5.233	0.010	0.011	0.010	0.011
Syringe #2	5.242	5.247	0.005		0.005	
Syringe #3	5.239	5.243	0.004		0.004	
Syringe #4	5.341	5.35	0.009		0.009	
Syringe #5	5.258	5.278	0.020		0.020	
Syringe #6	5.245	5.261	0.016		0.016	

4. CONCLUSION

The data presented in Tables 2 and 3 demonstrate that 6 doses can be delivered from the current BNT162b COVID-19 drug product vial when using Poonglim prototype low dead-space components (≥1.8 mL delivered volume, ≤ 35 µL dead-space).

5. REFERENCES

Keston, J. M. (2017). Acceptability of low dead space syringes and implications for their introduction: a qualititative study in the West of England. *Int J Drug Policy*, 39: 99-108.

Kume, T. (2012). The effects of different syringe volume, needle size and sample volume on blood gas analysis in syringes washed with heparin. *Biochemica Medica*, 22(2): 189-201.

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