BIOPHARMA GROUP APPLICATION NOTE

Optimising Bead Production: Dispensing Accuracy

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CHALLENGES:

Production of beads using samples with different viscosities can be challenging. Accurate dispensing is essential for ensuring technical precision, patient safety, regulatory compliance, and efficient resource utilisation. These factors are critical for producing a reliable and effective product.

However, getting accurate dispensing volume throughout the batch is not always possible. Samples with high viscosity can be difficult to dispense, and certain reagents, such as surfactants, may further complicate the process of achieving consistent droplet sizes.

Quality control (QC) checks conducted after the completion of the process of Lyobead production ensure its effectiveness and consistency across the entire batch. However, process efficiency can be significantly enhanced by optimising the production method to minimise the occurrence of faulty beads.

To assess dispensing accuracy and consistency before freeze-drying, an internal study was conducted using Biopharma Group's LyobeadPro instrument.

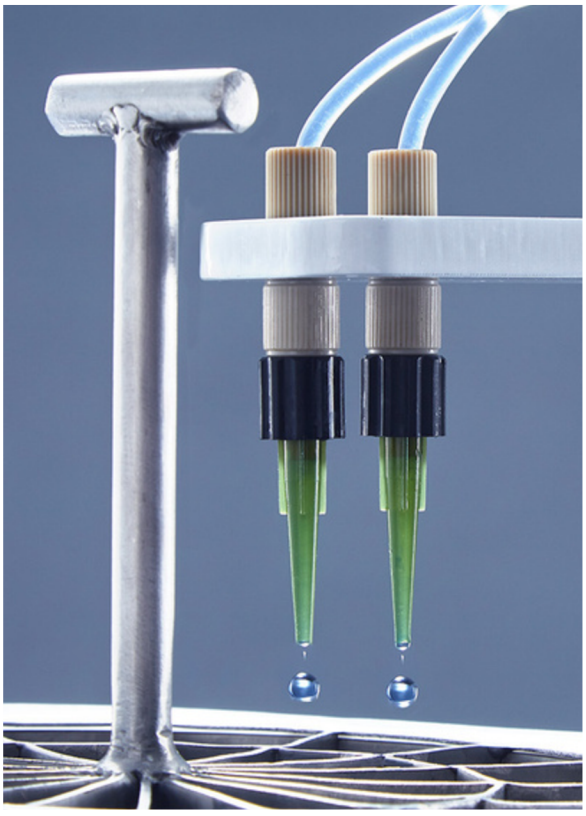

Figure 1: LyobeadPro instrument - Droplets during dispensing prior to freezing.

SOLUTION:

Using LyobeadPro, we can achieve highly accurate dispensing across most volume ranges by adjusting parameters such as nozzle size and rotation rate.

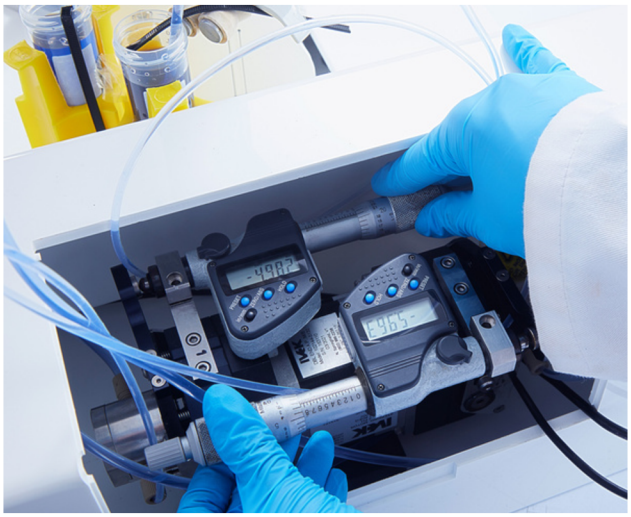

Figure 2: LyobeadPro Instrument - Adjusting the Dispensing Volume.

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METHOD:

Dispense parameters, including rotation rate and micrometre settings, were optimised. For samples with different densities, the average droplet volume was measured using an analytical lab balance, and the total number of dispenses was recorded.

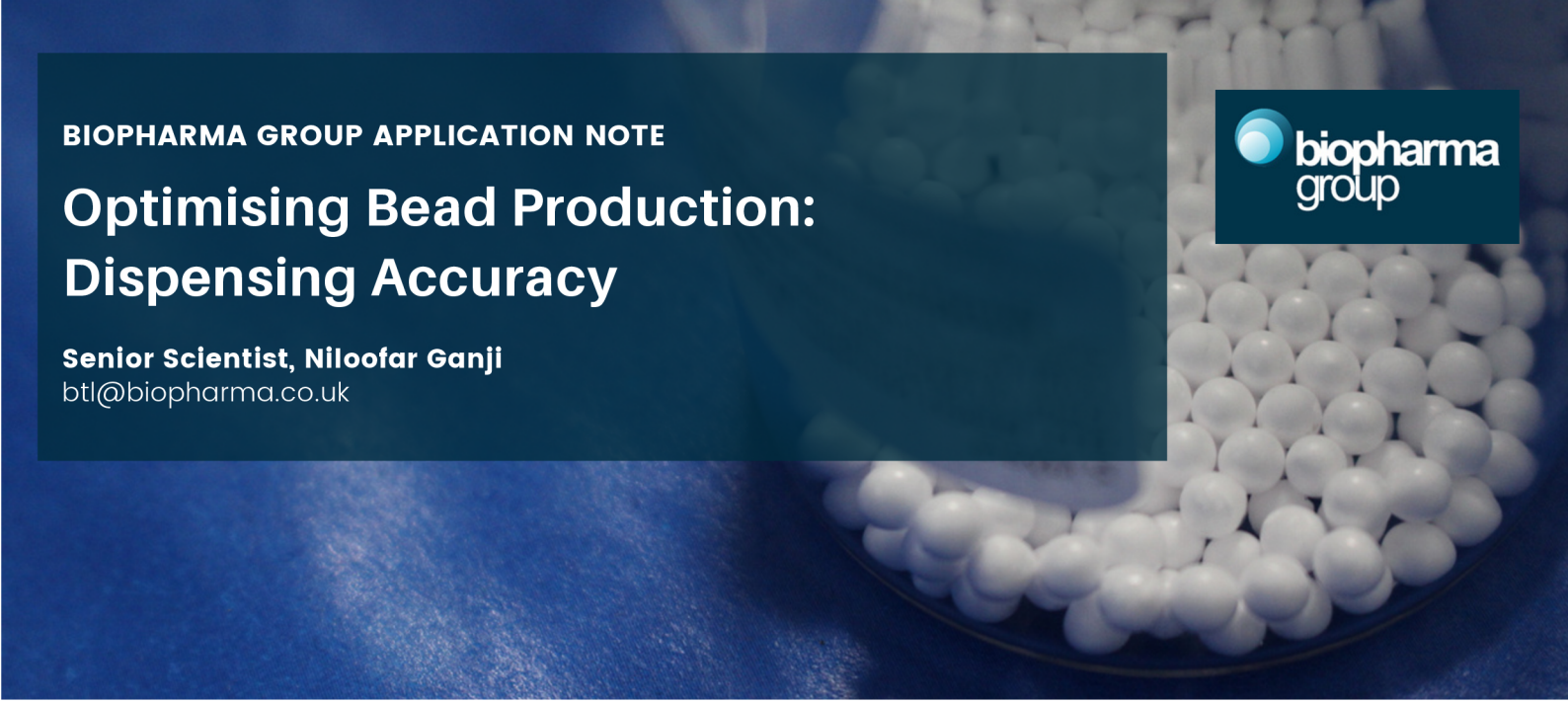
Various volumes of mixes with different densities were dispensed using Biopharma Group's LyobeadPro instrument.

The table below summarises the relationship between sample density and the coefficient of variation (CV%). A key experimental overview is as follows:

1. Density (g/cm³): The density of the samples ranges from 1.00 to 1.21 g/cm³.
2. Average Dispensed Volume: For each density value, different volumes (4 µL, 7 µL, and 15 µL) were dispensed during the experiments.
3. Number of Droplets: A constant number of 500 droplets was dispensed for each condition.
4. CV% (Coefficient of Variation): The CV% indicates the variability in droplet size for each condition:
    - At 1.00 g/cm³, the CV% is lower, particularly for the 15 µL volume (0.88%). Higher CV% of smaller volumes is due in part to having more challenges in recording data of smaller volumes as it would be easier to mishandle smaller volumes and impact of evaporation and surface tension effects on recording this data.
    - At higher densities (1.12 and 1.21 g/cm³), the CV% tends to increase, reflecting greater variability in droplet size as viscosity or sample properties change.

Density (g/cm³)	Average Dispensed Volume	Number of droplets	CV%
1.00	4 µL	500	1.71
	15 µL	500	0.88
1.12	4 µL	500	1.63
	15 µL	500	2.17
1.21	7 µL	500	2.80
	15 µL	500	2.87

Table 1: The density of all samples was mesaured under identical temperature conditions.



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RESULTS:

The data obtained from dispensing samples with varying densities using the LyobeadPro instrument demonstrate the system's precision and reliability. Across different densities and volumes, the coefficient of variation (CV%) remained consistently low, indicating high reproducibility and accuracy.

However, as the density of the sample increases, maintaining consistent droplet sizes (lower CV%) becomes more challenging, particularly at larger volumes. This trend underscores the importance of optimising dispensing parameters for different sample densities.

Building on the demonstrated precision and reliability of the LyobeadPro instrument, the platform's controllable parameters further enhance its ability to handle a wide range of viscosities effectively. This makes it a versatile tool for applications requiring precise dispensing in biopharmaceutical processes.