BIOPHARMA GROUP APPLICATION NOTE

Addressing the Challenges associated with Electrostatic Charge in Lyophilised Bead Production

Challenge

Producing lyophilised products, including spray freeze-dried materials and lyobeads, presents significant challenges related to electrostatic charging. Electrostatic charges can develop at various stages of the production process, with the product's formulation and packing environment playing a critical role in mitigating this issue.
Handling lyobeads can be difficult due to their low mass and static charge, causing them to cling to each other and contact surfaces, making separation and handling challenging and requiring special tools.

Additionally, the low density of the beads limits gravitational forces, making them very sensitive to airflow. This application note explains the sources of electrostatic charge and the correct processes to avoid it.

Figure 1
Lyobeads held at the bottom of the vial. The electrostatic charge generated by using glass vials is strong enough to prevent gravity from dislodging the lyobeads

Sources of Electrostatic Charge in Lyobead Production

Freeze-dried material can gain electrostatic charge through several mechanisms (Figure 1)

• Contact with Containers :

Lyobead samples may become charged when in contact with plastic or glass containers used during the freeze-drying process.

• Collection in an Isolator :

During the collection of lyobeads in an isolator, numerous energetic contacts with plastics used in the pick-and-place process can induce static charges.

Static charge can be more challenging when a plastic-based final container is used. This issue is exacerbated when lyobeads attach to the foil (seal) and may melt after the sealer is applied (Figure 2 and 3)

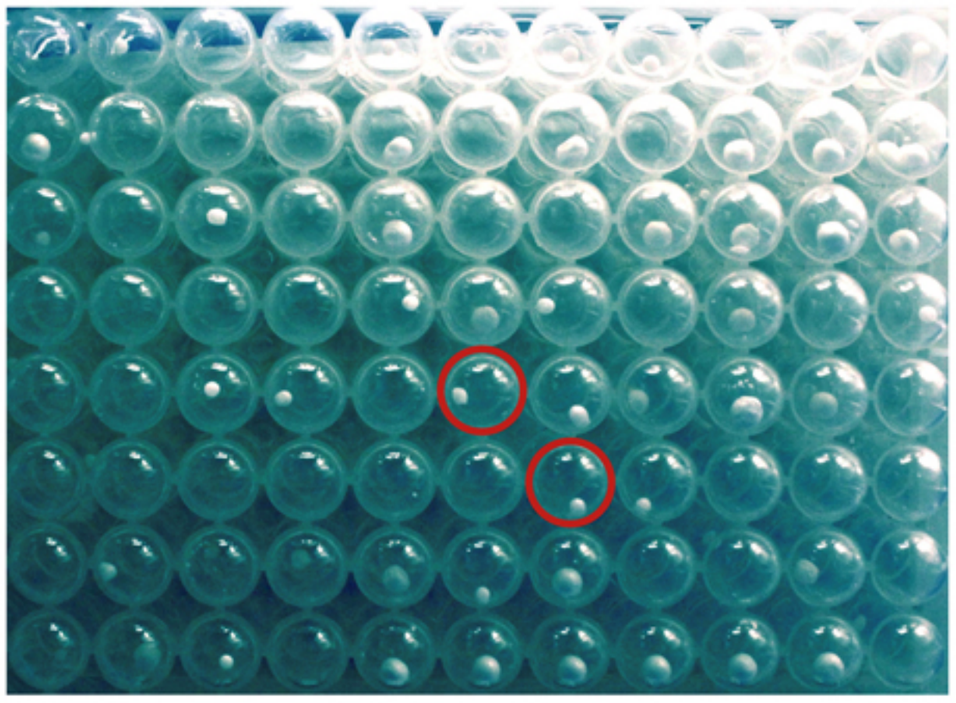

Figure 2
Lyobeads are attached to the foil due to static charge and melting during the sealing process

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Figure 3
Lyobeads remaining in the plastic container without any static charge and preventing attachment to the foil. This is achieved by using the correct handling method and avoiding static charge throughout the process

In certain pick-and-place methods, static charge can assist the packing process. If the method relies on static charge and it is unsuitable for a vacuum pen to directly contact the lyobead, static charge can effectively be used to lift the lyobead from the surface.

The Role of Long-Chain Molecules in Electrostatic Charge of Lyobeads

Long-chain molecules, such as starch, can significantly influence electrostatic charge due to (Figure 2) :

• Surface Area and Charge Distribution :

Long-chain molecules have large surface areas, increasing the likelihood of charge separation and accumulation during handling or processing

• Polarity and Dielectric Properties :

Polymers with polar functional groups or insulating properties can contribute to the build-up and retention of static electricity

• Interaction with Other Components :

These molecules may interact differently with other formulation components, leading to heterogeneous charge distribution

The combination of these factors contribute to the propensity of long-chain molecules to cause static build-up in dried materials. However, these molecules are often essential for improving the mechanical robustness of lyobeads. Biopharma Group has worked with several Lyobead customers to provide a good balance of favourable mechanical robustness and electrical properties.

Solutions to Prevent Static in Lyobeads

Several methods can prevent static in lyobeads, though modifying the formulation is preferable to fully resolve this issue :

• Use Metal Vials or Antistatic Containers for Freeze-Drying and Metal Tools to Handle Beads :

Studies show that glass vials or plastic spatulas can cause static charge in the beads metal vials or antistatic containers, due to their conductive properties, can help avoid static charge by allowing free electrons to flow easily across their surfaces, dissipating any static charge that builds up on the beads (Figure 4).

Figure 4
Using an antistatic container and metal vial to handle beads

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- **Use an Isolator with Minimal Plastic :**

Biopharma Group's (BG) isolator is primarily made of non-static material with a humidity-controlled environment. Antistatic gloves further reduce the chance of inducing electrostatic charge in the material (Figure 5).

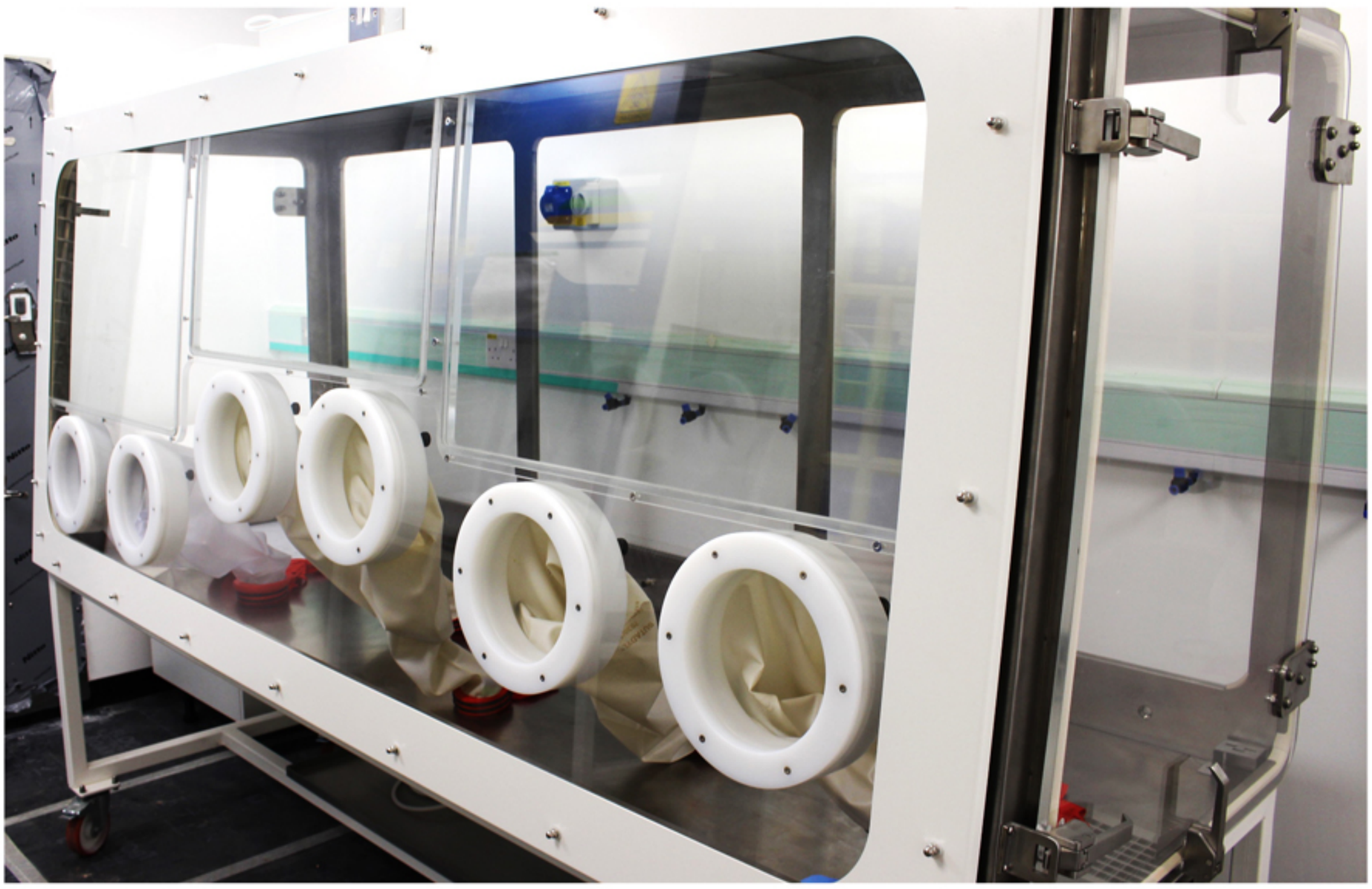

Figure 5
Biopharma Group's Isolator equipped with temperature control and humidity control made from metal, other antistatic materials and antistatic gloves

Conclusion

Using the correct methods of handling lyobeads can significantly mitigate risks associated with the packing process, even when long-chain molecules are used in the formulation. Customers can benefit from Biopharma Group's expertise in formulation and post-lyo handling techniques which are crucial in overcoming the electrostatic issues encountered in lyophilised bead production.

References

1. Jayaprakash P. et al. (2023) Comparison of electrostatic spray drying, spray drying, and freeze drying for lacticaseibacillus rhamnosus GG dehydration, MDPI

2. Lin EY, Frischknecht AL, Winey KI, Riggleman RA. Effect of surface properties and polymer chain length on polymer adsorption in solution. Chem Phys. 2021 Jul 21;155(3):034701

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