

The Strategic Value of In-House Delumping for Homogeneous API Production

Improving quality, efficiency, and risk control in pharmaceutical powder processing.

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Introduction

Delumping is an established operation in pharmaceutical manufacturing for producing more homogeneous, free-flowing powders in both drug substance and drug product processes. Powders discharged from dryers can show varying degrees of heterogeneity as a result of intrinsic material properties, dryer geometry, mixing efficiency, residual solvent content, and handling history. When not addressed, agglomeration can impair charging, flowability, homogeneity, compatibility with downstream equipment, cycle time, and yield. By implementing in-house delumping at its Drug Substance site in Oss, Ardena has strengthened its ability to de-risk solids handling, improve operational efficiency, and support robust development-to-GMP manufacturing for challenging API powders.

The Importance of Homogeneous API Batches

Homogeneity in API batches is fundamental to pharmaceutical quality. Consistent particle characteristics and composition support downstream formulation, process scalability, representative sampling, and regulatory compliance. Variability in powder behavior can complicate dispensing, blending, feeding, and packaging, and may ultimately affect the manufacturability and performance of the final drug product.

Delumping is the controlled breakdown of agglomerates within a powder batch to restore flow, improve chargeability, and reduce variability without unnecessarily reducing primary particle size. Agglomerates may arise from moisture uptake, incomplete drying, compaction during handling, or storage effects. If left unaddressed, they can compromise sampling consistency, analytical reliability, dosing accuracy, and downstream process robustness, and in severe cases contribute to rework or batch failure.

Advantages of In-House Delumping

Cost Savings

Delumping is often outsourced, which adds shipping, handling, coordination, and service costs to a project. Bringing this capability in-house reduces those external

dependencies while giving Ardena greater planning flexibility by integrating delumping directly into the manufacturing workflow.

Reduced Project Timelines

Performing delumping on site can shorten project timelines by removing inter-facility transfers and external scheduling delays. This enables faster progression from drying to downstream unit operations, improves responsiveness when powder behavior differs from expectations, and helps keep development and GMP campaigns on track.

Risk Mitigation

In-house processing also reduces operational risk. External transfers can expose API batches to contamination, temperature excursions, physical damage, administrative complexity, and chain-of-custody challenges. Keeping the operation within Ardena's controlled environment helps protect product integrity, support traceability, and reduce the need for manual ad hoc lump breaking, improving robustness, operator ergonomics, and alignment with quality-by-design principles.

Equipment Overview: CC-L1006 DELUMP-01 Quadro SLS

Mill

The Quadro SLS (Scalable Lab System) is a compact milling and screening platform designed for rapid, efficient powder processing at laboratory and small manufacturing scale. Its modular design, based on interchangeable processing heads and screens, allows the system to be configured quickly for specific materials and campaign needs. At Ardena Oss, the unit is configured with the U5 Comil head, in which powder is guided through a conical screen by a rotating impeller to break down agglomerates into a more uniform, free-flowing material.



Figure 1: Picture of a Quadro SLS mill with U5 Comil® head

This approach is well suited to controlled de-agglomeration, helping restore flow and chargeability while avoiding unnecessary particle size reduction. For the U5 Comil head on the Quadro SLS, the allowable operating range is 1750–6500 RPM. Processing speed is selected for each material to balance effective delumping with the desired powder attributes. In routine delumping mode, a screen configuration delivering an output of approximately 1000 µm can serve as a practical starting point, while alternative screen types and sizes can be selected when project requirements call for different outcomes.

- Model: CC-L1006 DELUMP-01 Quadro SLS mill.
- Current configuration: U5 Comil head for controlled delumping and coarse milling of agglomerated powders.
- Speed range: 1750–6500 RPM for the U5 configuration.
- Screen flexibility: Multiple screen types and opening sizes are available to accommodate different powder behaviors and target outcomes.
- Modularity: The SLS platform can be equipped with alternative processing heads and impeller profiles, extending capability beyond the standard U5 set-up.
- Scalability: Suitable for development, non-GMP and GMP manufacturing, including highly potent programs.

What This Enables at Ardena Oss

The CC-L1006 delumping capability strengthens Ardena Oss's offering for challenging solids handling and helps clients reduce variability without introducing additional subcontractors. Key applications include improving powder flow by breaking up lumps formed during drying, reducing bridging and ratholing

in bags or containers, replacing manual lump breaking with a controlled and repeatable unit operation, and establishing a consistent pre-processing step that supports smoother downstream feeding, blending, charging, and packaging.

Client Benefits in Practice

- More predictable downstream processing with fewer unplanned stops.
- Reduced risk of rework and handling losses.
- A scalable approach from development to GMP, including highly potent material.
- An end-to-end drug substance pathway under one roof, reducing coordination delays.

Performance Demonstration: Delumping of Lactose Monohydrate

As part of equipment qualification, Ardena Oss performed an initial delumping demonstration using lactose monohydrate as a representative powder. To challenge the set-up, a portion of the lactose was intentionally wetted with demi-water (5% w/w) to create visible agglomerates and then stored overnight to allow full absorption. The material was processed on CC-L1006 at 1750 RPM, the minimum operating speed for the U5 configuration on this platform. The run was completed smoothly and produced a free-flowing powder, demonstrating that effective de-agglomeration can be achieved under relatively gentle conditions.

Quality and GMP Readiness

CC-L1006 DELUMP-01 is installed and qualified for GMP-relevant use as a delumping unit for dry, powdery substances. Operation, cleaning, and maintenance are performed under controlled procedures with full traceability through batch documentation. To support efficient and compliant campaign changeovers, cleaning validation has been completed for the delumper, with residue removal verified by visual inspection and analytical testing when executed according to the validated process.



Figure 2: Before delumping



Figure 3: After delumping

Processing of High-Potency Material (OEB-5): Client Demonstration and GMP Batch

Following qualification, the CC-L1006 was successfully deployed on a client program involving high-potency material (OEB-5). Both a demonstration batch and a subsequent GMP batch were delumped without issue. The operation ran smoothly and produced visibly more uniform material, as illustrated in Figures 2 and 3. A yield of 98% was achieved, underscoring Ardena's readiness to support GMP campaigns for highly potent compounds with a robust and reliable delumping step.

Conclusion

By implementing the CC-L1006 DELUMP-01 Quadro SLS mill, Ardena Oss has added a qualified, flexible in-house delumping capability that helps clients de-risk solids handling, reduce dependence on external subcontractors, and improve downstream processing performance. Qualification work, a representative lactose demonstration, and successful client application with highly potent OEB-5 GMP material show that effective delumping can be achieved under controlled conditions while maintaining operational efficiency and high yield. Together, these outcomes strengthen Ardena Oss's ability to support robust, efficient development-to-GMP campaigns in which powder flow, handling, and consistency are critical to success.



References

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