

TABLETING | GRANULATION

MILLED LACTOSE

Technical brochure

General information

Crystalline alpha-lactose monohydrate grades have a long tradition in pharmaceutical applications due to their chemical and physical stability, in oral, parenteral and inhalative pharmaceutical applications, versatile binder-filler properties, and global availability [1]. Milling alpha-lactose monohydrate to different particle size distributions offers multiple opportunities to tailor its physical characteristics and functional performance.

During the milling process, finer, sharper-edged particles are formed, having cohesive powder properties that can be beneficial during granulation processes. Clean unlubricated surfaces created during the compaction process as a result of brittle fracture lead to improved compactibility [2].

MEGGLE's milled alpha-lactose monohydrate grades have a long-standing history of successful use as reliable diluents in dry and wet granulation processes by pharmaceutical manufacturers worldwide.

Brittle alpha-lactose monohydrate exhibits good binding properties, and consolidates mainly by fragmentation, but particle flow of milled lactose grades is moderate, depending on size and its corresponding specific surface.

Its particle size distribution and associated specific surface area can be selected to tailor granule characteristics and downstream tablet performance, including tablet strength and disintegration behavior.

Milled lactose grades therefore provide a versatile platform for a broad range of pharmaceutical applications. Their particle characteristics can be further modified through agglomeration – an established approach to improve flowability through gentle particle size enlargement. This process forms the basis of MEGGLE's agglomerated Tablettose® product family.

MEGGLE's milled lactose grades are generated by a well-defined manufacturing process resulting in a clearly specified particle size distribution.

Product description

A range of milled lactose grades with distinct physical characteristics is available to support diverse pharmaceutical applications. The following chart provides recommended areas of application.

APPLICATION

Milled lactose

- Dry Granulation
- Wet Granulation
- Continuous applications
- Powder blends, premixes
- Triturations (low dose API, colorants etc.)
- Fermentation Media
- And more

The milled lactose product family offers a broad range of grades with different particle size distributions (PSDs), allowing optimal matching to specific API characteristics and formulation requirements.

BENEFITS

Milled lactose

- Granules with very good tableability
- Adjustable tablet properties: finer lactose grades can enable higher tablet strength and faster dissolution
- Low and consistent water amount required for granulation
- Fast drying, less energy
- Double source of GranuLac® 70, 140, 200 (German and US site)
- Defined particle size distribution
- Good blending properties
- High storage stability
- High batch-to-batch consistency

MEGGLE Low Nitrite grades

Due to the nitrosamine issue, the risk assessment and review of nitrite content in excipients have become essential. Pharmaceutical manufacturers must take appropriate measures, especially for critical products. MEGGLE supports manufacturers by offering Low Nitrite grades with nitrite content measured for every production lot. The specified nitrite limit is part of the official product specification and the corresponding Certificate of Analysis (CoA), making risk assessments easier and ensuring compliance with regulatory expectations.

Regulatory & quality information

MEGGLE's milled (GranuLac® 70, GranuLac® 80, GranuLac® 140, GranuLac® 200, GranuLac® 230, SorboLac® 400) alpha-lactose monohydrate grades comply with the current harmonized Ph. Eur., USP-NF, JP and ChP monographs. Specifications and regulatory documents can be downloaded from www.meggle-excipients.com.

MEGGLE offers a broad portfolio of lactose grades meeting pharmaceutical standards with several being dual sourced (Wasserburg am Inn, Germany and Le Sueur, USA).

Our pharma-dedicated production facility in Wasserburg am Inn, Germany, is certified according to DIN EN ISO 9001 and has implemented GMP according to the Joint IPEC-PQG (Good Manufacturing Practices Guide for Pharmaceutical Excipients) and USP-NF General Chapter <1078> GOOD MANUFACTURING PRACTICES FOR BULK PHARMACEUTICAL EXCIPIENTS. MEGGLE has been an EXCiPACT™-certified excipient manufacturer and supplier since 2014.

The Wasserburg facility demonstrates MEGGLE's complete lactose production capability range, including sieving, milling, agglomeration, spray-drying, and co-processing. The US site in Le Sueur, Minnesota produces to equivalent quality standards and provides the same documentation. Additionally MEGGLE is a member of IPEC (International Pharmaceutical Excipients Council).

MEGGLE invests considerably in the sustainability of raw material sourcing, production standards, and efficiency. We are actively engaged in environmental protection. In order to guarantee the quality of our products, our commitment and adherence to established pharmaceutical standards is our highest priority.



Particle Size Distribution (PSD)

MEGGLE's crystalline alpha-lactose monohydrate grades are available in various PSDs according to the diversified needs of our customers. **Figure 1** shows typical laser diffraction particle size distribution data for MEGGLE's milled lactose grades.

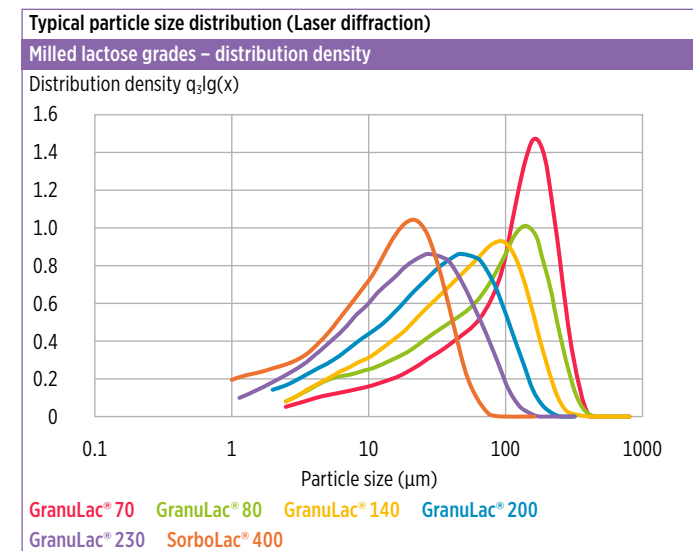
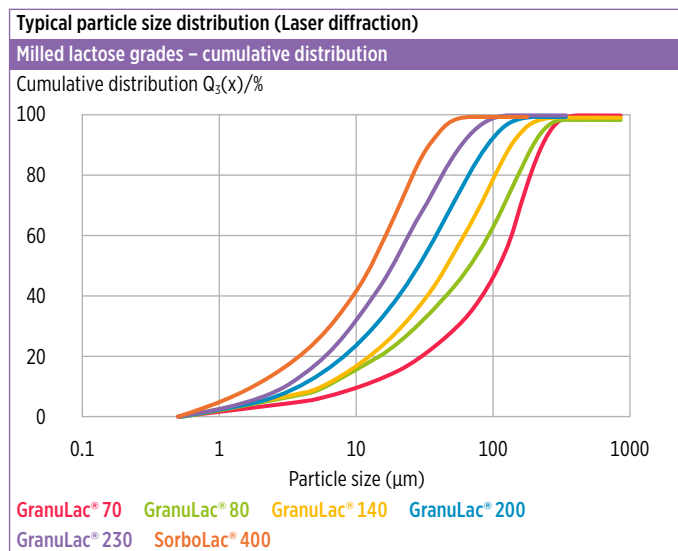


Figure 1: Typical cumulative PSD and distribution density of MEGGLE's milled lactose grades GranuLac® 70, 80, 140, 200, 230 and SorboLac® 400.

Analyzed by Sympatec®/Helos & Rodos particle size analyzer.

Particle Size Distribution (PSD) & Morphology (SEM)

Figure 2 depicts the specified PSD range and typical average values for MEGGLE's milled grades, and their typical Scanning Electron Microscope (SEM) images.

These parameters are constantly monitored through in-process control (IPC) testing and are part of milled MEGGLE lactose grades' PSD specification obtained using air-jet sieving.

Milled lactose grades show different morphology, as it can be seen in the different SEM pictures. Their disrupted and sharp-edged appearance derives from a defined milling process.

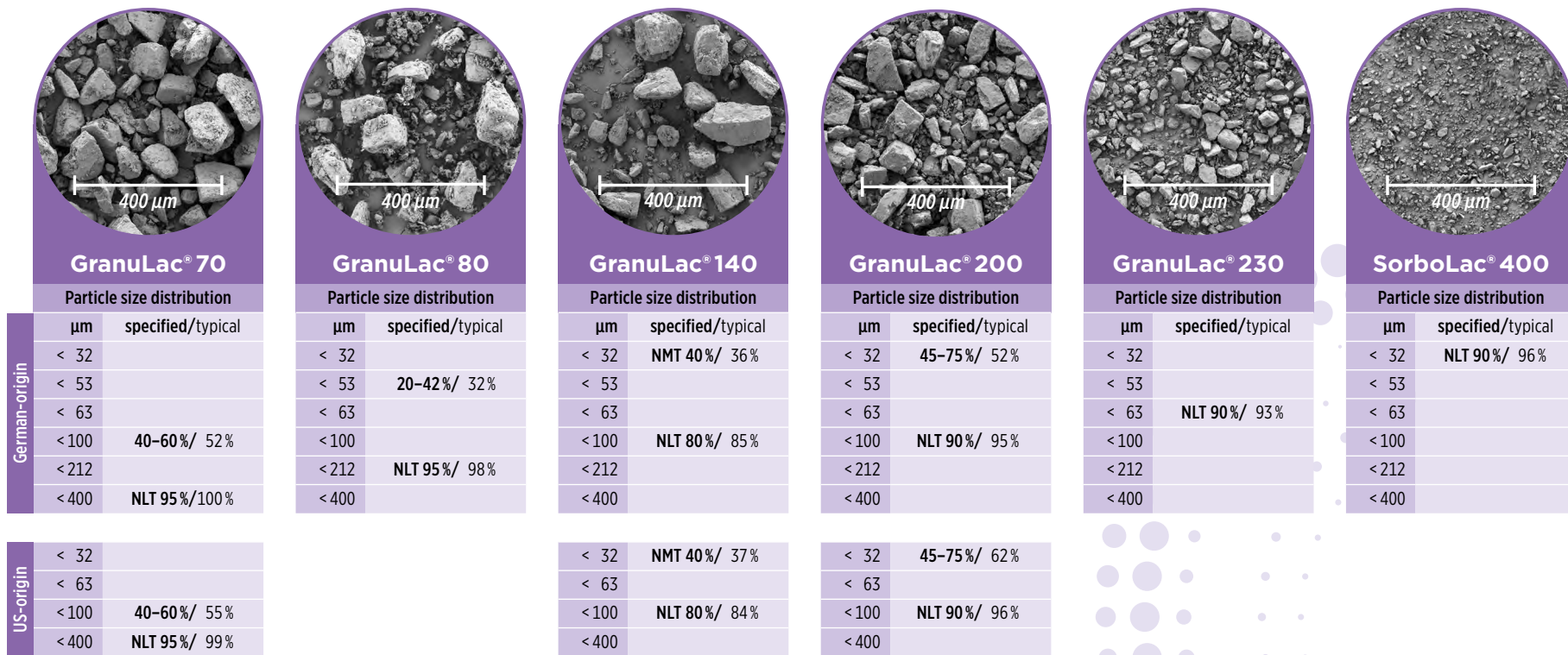


Figure 2: Specified PSD ranges for MEGGLE's milled lactose grades by air-jet sieving in bold letters. Typical values obtained from a permanent in-process control are shown for orientation.

SEM images of various milled MEGGLE lactose grades by ZEISS Ultra 55 FESEM (U = 5 kV; Au/Pd sputtered).

Functional related characteristics – Part 1

The granulation method significantly influences the flowability of milled lactose powders. Dry granulation can enhance flow by increasing particle size and reducing dust content, although it often results in more irregular particle shapes and a broader size distribution, which may limit flow uniformity. In contrast, wet granulation typically leads to improved flowability by producing more spherical and uniform granules with fewer fines [3].

Specific surface

The degree of milling affects not only the particle size distribution but also the specific surface area. As shown in figure 3, finer milling results in higher specific surface area values. The increased surface area enhances the potential for interparticulate bonding, which can improve granule strength and supports the uniform distribution of the API during blending.

Specific surface area determination by BET	
Milled lactose	
	(m ² /g)
GranuLac® 70	0.3
GranuLac® 80	0.5
GranuLac® 140	0.6
GranuLac® 200	1.0
GranuLac® 230	1.2
SorboLac® 400	1.9

Figure 3: Typical specific surface areas of milled MEGGLE lactose grades. Determined by multipoint BET nitrogen adsorption using a QuadraSorb instrument (Quantachrome).

Wet and dry granulation

Milled lactose grades have a long-established role in dry granulation processes, including roller compaction and slugging. Both processes involve an initial compaction step followed by milling to produce granules for final tableting. In roller compaction, force feeding reduces the impact of moderate powder flowability.

For low-dose formulations, trituration of the API with fine GranuLac® grades can support content uniformity by promoting homogeneous API distribution and minimizing segregation. For formulations containing challenging APIs or high API loadings, however, flowability may become a limiting factor – particularly when fine lactose grades are required to provide adequate binding. In such cases, wet granulation can be a beneficial alternative to improve flowability and ensure robust granule formation.

MEGGLE offers milled lactose grades with a broad range of particle sizes, enabling formulation-specific optimization of flowability and binding strength.

Extrusion/spheronization processes also make use of milled lactose as a filler.

Functional related characteristics – Part 2

Powder flow

Powder flow is an important functional characteristic in formulation development and product manufacturing. Differences in morphology and PSD of milled lactose grades maintain discrete flow performances: According to Ph. Eur. there are different gradations to define flow property of a powder (**Figure 4**).

Classification of powder flow according to Ph. Eur.		
Flow property	Carr's Index (%)	Hausner ratio
Excellent	1 – 10	1.00 – 1.11
Good	11 – 15	1.12 – 1.18
Fair	16 – 20	1.19 – 1.25
Passable	21 – 25	1.26 – 1.34
Poor	26 – 31	1.35 – 1.45
Very poor	32 – 37	1.46 – 1.59
Very, very poor	> 38	> 1.60

Figure 4: Calculation of the CI and the Hausner ratio. Classification according to Ph. Eur. 2.9.36. A CI below 11 and a Hausner Ratio below 1.12 implies excellent flow property of the material. A value between 21 – 25 (CI) and 1.26 – 1.34 (Hausner Ratio) implies passable flow property.

$$\text{Carr's Index (CI)} = \left(\frac{\rho_{\text{tapped}} - \rho_{\text{bulk}}}{\rho_{\text{tapped}}} \right) \times 100$$

$$\text{Hausner ratio} = \left(\frac{\rho_{\text{tapped}}}{\rho_{\text{untapped}}} \right)$$

Figure 5 shows typical flowability indices for MEGGLE's milled lactose grades. All milled lactose grades show poor flowability, with CI values between 25 – 36 % and a Hausner ratio between 1.33 and 1.56.

Flowability				
Milled lactose				
	Carr's Index (%)	Hausner ratio	Density bulk (g/l)	Density tapped (g/l)
GranuLac® 70	25	1.33	715	952
GranuLac® 80	33	1.49	641	955
GranuLac® 140	32	1.47	628	906
GranuLac® 200	37	1.59	532	844
GranuLac® 230	35	1.54	501	768
SorboLac® 400	36	1.56	437	681

Figure 5: Typical technological values, describing powder flowability, shown for milled MEGGLE lactose grades.

Figure 6 shows the CI of MEGGLE's milled grade lactose. Due to its coarser PSD, GranuLac® 70 shows better flowability compared to the finer grades. Additionally, all grades exhibit significantly lower CI values after granulation ("granules"), which can be attributed to particle agglomeration.

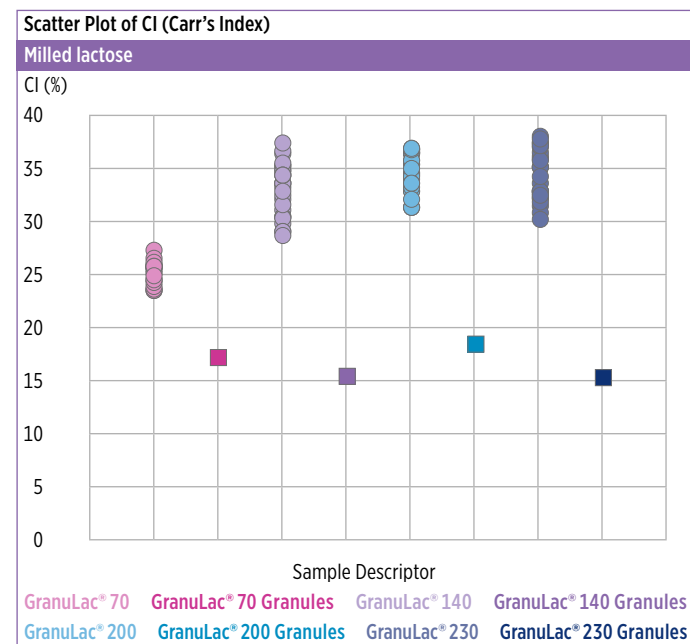


Figure 6: Carr's Index of MEGGLE's milled lactose grades in comparison with produced granules of MEGGLE's milled grades with 0.5 % Povidone.

Batch-to-batch consistency

Batch-to-batch consistency for all lactose products can be attributed to MEGGLE’s long history and experience in lactose manufacturing, and broad technical expertise. Constant in-process and final product testing ensures consistency and quality. For detailed information: www.meggle-excipients.com.

Isotherm

MEGGLE’s milled alpha-lactose monohydrate products do not adsorb significant amounts of water below 90 % relative humidity at 25 °C (non-hygroscopic). **Figure 7** shows sorption and desorption isotherm for GranuLac® 200.

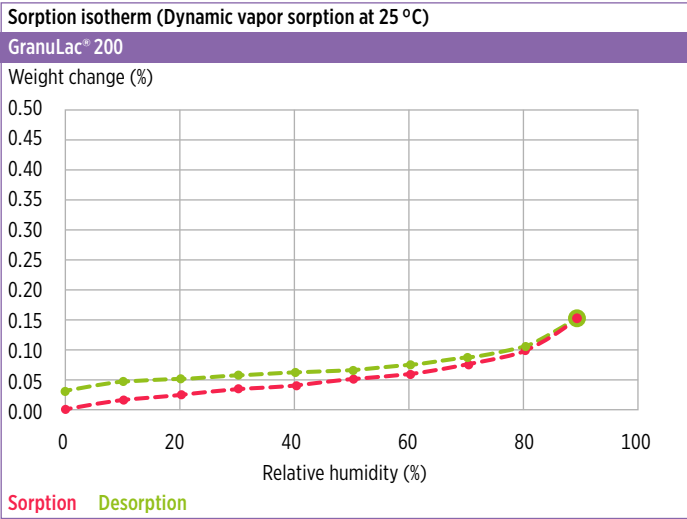


Figure 7: Sorption-desorption isotherms (25 °C) of alpha-lactose monohydrate, using GranuLac® 200 as an example. Analysis performed with SPSx-1µ Advance (proUmid GmbH & Co. KG, Ulm, Germany)

Packaging and shelf life

Packaging material complies with Regulation (EC) No.1935/2004 and 21 CFR 174, 175, 176, 177 and 178. Stability tests have been performed according to ICH guidelines and an ongoing stability program is implemented. **Figure 8** provides an overview about packaging size and material, and product shelf life.

Packaging and shelf life			
Milled lactose			
	Size	Material	Shelf life
GranuLac® 70	25 kg	Paper bag with PE-EVOH-PE inliner	36 Months
GranuLac® 80			
GranuLac® 140			
GranuLac® 200			
GranuLac® 230	20 kg	Paper bag with an aluminum-laminated inliner	24 Months
SorboLac® 400			36 Months

Figure 8: Packaging and shelf life of MEGGLE’s milled lactose grades.

Literature

- [1] Armstrong, N. A. (2007) Tablet manufacture. Encyclopedia of Pharmaceutical Technology, Ed. Swarbrick J., informa healthcare, New York, London: 3653.
- [2] Vormans, H., De Boer, A. H., Bolhuis, G. K., Lerk, C. F., Kussendrager K. D., and Bosch, H. (1985) Pharm. Weekblad Sci. 7: Studies on tableting properties of lactose: 186 – 193. link.springer.com
- [3] Smith, J., & Jones, A. (2017). The effect of dry granulation on flow behaviour of pharmaceutical powders during die filling. International Journal of Pharmaceutics, 530(1–2), 123–131. sciencedirect.com

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