



MILLED AND

GRANULAC® 70
GRANULAC® 80
GRANULAC® 140
GRANULAC® 200
GRANULAC® 230
SORBOLAC® 400

SIEVED LACTOSE

PRISMALAC® 40
CAPSULAC® 60
SACHELAC® 80
SPHEROLAC® 100

**Technical brochure
Milled and sieved lactose**

MEGGLE's crystalline alpha-lactose monohydrate grades: Milled and sieved

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]. Impacting recrystallized alpha-lactose monohydrate particles by either a milling or sieving during production opens multiple opportunities to influence 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 been historically used as diluents in dry and wet granulation processes by numerous global and regional pharmaceutical manufacturers.

Narrow fractionation of randomly sized lactose crystals results in coarse sieved grades, which show particle size and shape-dependent powder flow for increased production speeds. MEGGLE's sieved alpha-lactose monohydrate grades are mainly monocrystals with some agglomerates, exceptionally suited to permit and optimize applications where powder flow is important.

MEGGLE's sieved and milled lactose grades are generated by a well-defined manufacturing process resulting in a high degree of crystallinity.

Regulatory & quality information

MEGGLE's milled (GranuLac® 70, GranuLac® 80, GranuLac® 140, GranuLac® 200, GranuLac® 230, SorboLac® 400) and sieved (PrismaLac® 40, CapsuLac® 60, Sachelac® 80, SpheroLac® 100) alpha-lactose monohydrate grades comply with the current harmonized Ph. Eur., USP-NF and JP 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, Germany and Le Sueur, USA).

Our pharma-dedicated production facility in Wasserburg, Germany is certified according to DIN ISO 9001:2015 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 remains our highest priority.



international excipients
certification

Application

Milled and sieved lactose grades exhibit significant physical characteristic differences, and as a result, vary in their application. The following chart provides recommended areas of application.

| Areas of application | | | | | | | | |
|---------------------------|-----------------|--------------------|-----------------|-----------------|---|-------------------------|------------------------|--------------------------|
| Milled/sieved lactose | | | | | | | | |
| Alpha-lactose monohydrate | Capsules | Tablets | | | Powder blends | Others | | |
| | Capsule filling | Direct compression | Dry granulation | Wet granulation | Blends, premixes, sachets, triturations | Enhancement of flavours | Media for fermentation | Extrusion-spheronization |
| Milled | ○ | – | + | + | + | + | + | + |
| Sieved | + | – | – | – | + | – | – | – |

+ = Highly suitable ○ = Suitable – = Poor performance/not recommended

BENEFITS

| Milled | Sieved |
|---|---|
| <ul style="list-style-type: none"> – Good compactibility – Narrow particle size distribution – Good blending properties – High storage stability – High batch-to-batch consistency | <ul style="list-style-type: none"> – Excellent flowability – Narrow particle size distribution – Good blending properties – High storage stability – High batch-to-batch consistency |

Particle size distribution (PSD)

MEGGLE's crystalline alpha-lactose monohydrate grades are available in various PSDs according to the diversified needs of our customers. **Figures 1 and 2** show typical laser diffraction particle size distribution data for MEGGLE's milled and sieved lactose grades.

Figures 3 and 4 depict the specified PSD range and typical average values by air-jet sieving (milled) and mechanical sieve shaker (sieved). These parameters are constantly monitored through in-process control (IPC) testing and are part of milled and sieved MEGGLE lactose grades' particle size distribution specification.

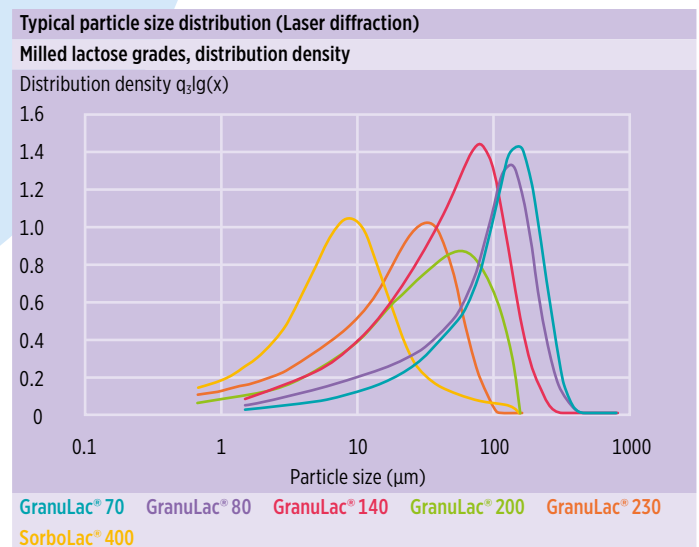
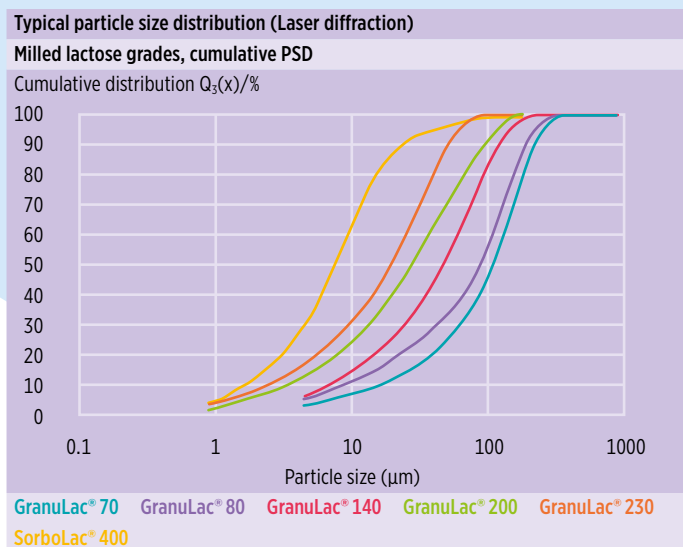


Figure 1: Typical cumulative PSD and distribution density of MEGGLE's milled lactose grades GranuLac® 70, 80, 140, 200, 230 and SorboLac® 400. Analyzed by Sympatec®/Helos & Rodos particle size analyzer.

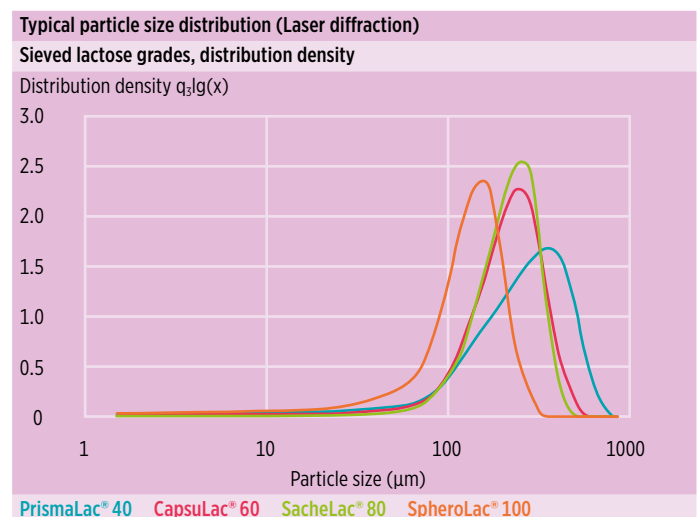
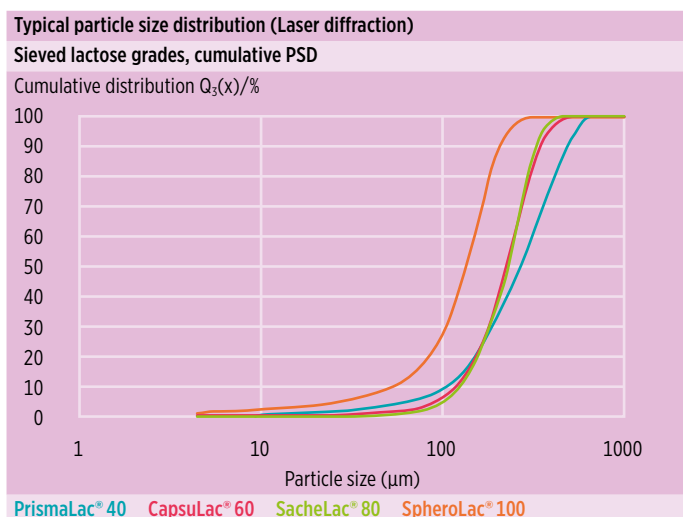


Figure 2: Typical cumulative PSD and distribution density of MEGGLE's sieved lactose grades PrismaLac® 40, CapsuLac® 60, Sachelac® 80 and Spherolac® 100. Analyzed by Sympatec®/Helos & Rodos particle size analyzer.

| Sieve data – milled lactose (German-origin) | | | | | | | |
|---|--------------|-----------------------------------|-----------------------------------|------------------------------------|------------------------------------|------------------------------------|------------------------------------|
| | Lactose type | GranuLac® 70 specified/typical | GranuLac® 80 specified/typical | GranuLac® 140 specified/typical | GranuLac® 200 specified/typical | GranuLac® 230 specified/typical | SorboLac® 400 specified/typical |
| Particle size distribution | < 32 µm | | | NMT 40%/34% | 45–75%/53% | / 74% | NLT 90%/ 98% |
| Method: | < 52 µm | | 20–42%/31% | | | | |
| Air-jet sieving | < 63 µm | | | | | NLT 90%/ 98% | /100% |
| | < 100 µm | 40–60%/ 51% | | NLT 80%/87% | NLT 90%/95% | /100% | |
| | < 212 µm | | NLT 95%/98% | | | | |
| | < 400 µm | NLT 95%/100% | | | | | |

Figure 3.1: Specified PSDs for MEGGLE's milled lactose grades by air-jet sieve in bold letters. Typical values obtained from a permanent in-process control are shown for orientation.

| Sieve data – milled lactose (US-origin) | | | | |
|---|--------------|---------------------------|----------------------------|----------------------------|
| | Lactose type | GranuLac® 70 specified | GranuLac® 140 specified | GranuLac® 200 specified |
| Particle size distribution | < 32 µm | | NMT 40% | 45–75% |
| Method: | < 63 µm | | | |
| Air-jet sieving | < 100 µm | 40–60% | NLT 80% | NLT 90% |
| | < 400 µm | NLT 95% | | |

Figure 3.2: PSD for MEGGLE's milled lactose grades (US manufacturing site), specified by air-jet sieving.

| Sieve data – sieved lactose (German-origin) | | | | | |
|---|--------------|------------------------------------|-----------------------------------|-----------------------------------|-------------------------------------|
| | Lactose type | PrismaLac® 40 specified/typical | CapsuLac® 60 specified/typical | SacheLac® 80 specified/typical | SpheroLac® 100 specified/typical |
| Particle size distribution | < 63 µm | | | | NMT 20%/ 9% |
| Method: | < 100 µm | | NMT 10%/ 3% | NMT 20%/ 3% | |
| Mechanical sieve shaker | < 150 µm | | / 9% | | / 70% |
| | < 200 µm | NMT 10%/ 4% | | | NLT 75%/ 97% |
| | < 250 µm | | 40–70%/50% | /51% | /100% |
| | < 400 µm | | NLT 90%/99% | NLT 98%/99% | |
| | < 500 µm | / 58% | | | |
| | < 630 µm | / 88% | NLT 97% | | |
| | < 800 µm | NLT 97%/100% | | | |

Figure 4: Specified PSDs for MEGGLE's sieved lactose grades by mechanical sieve shaker in bold letters. Typical values obtained from a permanent in-process control are shown for orientation.

Batch-to-batch consistency

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

Isotherms

MEGGLE's milled and sieved alpha-lactose monohydrate products do not adsorb significant amounts of water below 20 °C/90% relative humidity. **Figure 5** shows sorption and desorption isotherm for GranuLac® 200.

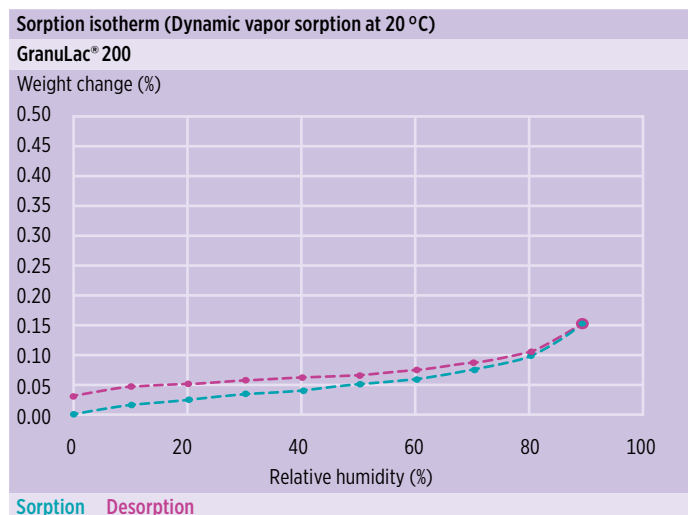


Figure 5: Sorption-desorption isotherms (20 °C) of alpha-lactose monohydrate, using GranuLac® 200 as an example. Analysis performed by SPSx-µ moisture sorption test system.

Scanning electron micrograph (SEM)

Milled and sieved lactose grades show different morphology. Where sieved products are mainly defined by coarse tomahawk-shaped monocystals and, to a minor extent, agglomerated particles, milled lactose grades consist of fine lactose particles. Their disrupted and sharp-edged appearance derives from a defined milling process (figure 6).

MILLED



Figure 6: SEM images of various milled and sieved MEGGLE lactose grades by ZEISS Ultra 55 FESEM (U=5 kV; Au/Pd sputtered).

SIEVED

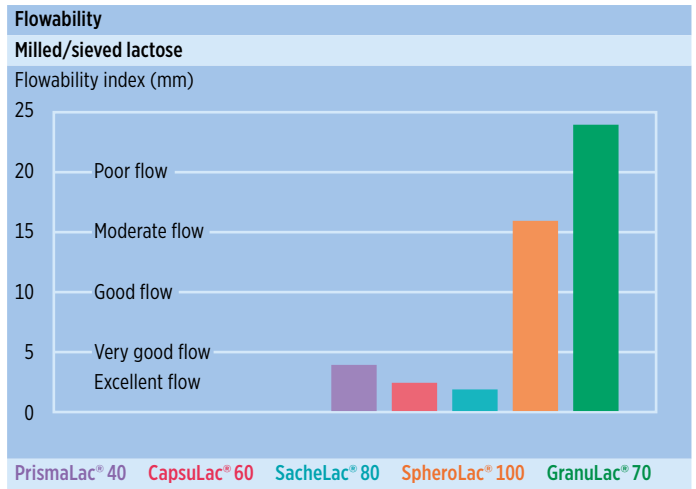
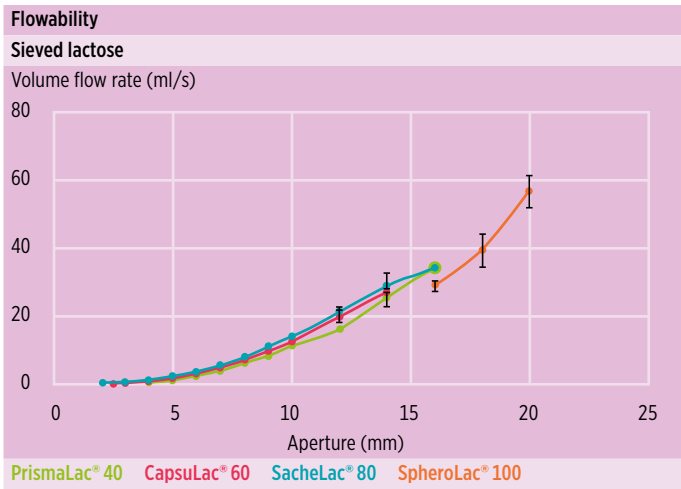
Functional related characteristics

Powder flow

Powder flow is an important functional characteristic in formulation development and product manufacture. Differences in morphology and PSD of sieved and milled lactose grades maintain discrete flow performances: Sieved lactose grades exhibit a better flow than milled ones, which can be quantified by methods as the angle of repose, bulk density derived factors or the volume flow/flowability index via a FlowRatex® (figures 7, 8 and 9).

| Flowability | | | | | |
|-----------------------|---------------------|--------------------|----------------------|---------------|------------------|
| Milled/sieved lactose | Angle of repose (°) | Density bulk (g/l) | Density tapped (g/l) | Hausner ratio | Carr's index (%) |
| | | | | | |
| GranuLac® 70 | 43 | 710 | 910 | 1.28 | 22 |
| GranuLac® 80 | - | 670 | 950 | 1.42 | 30 |
| GranuLac® 140 | 52 | 630 | 890 | 1.41 | 29 |
| GranuLac® 200 | 55 | 530 | 820 | 1.55 | 35 |
| GranuLac® 230 | 56 | 460 | 760 | 1.65 | 39 |
| SorboLac® 400 | 52 | 330 | 590 | 1.79 | 44 |
| Sieved | | | | | |
| PrismaLac® 40 | 34 | 440 | 540 | 1.23 | 19 |
| CapsuLac® 60 | 33 | 570 | 700 | 1.23 | 19 |
| Sachelac® 80 | 32 | 570 | 710 | 1.25 | 20 |
| SpheroLac® 100 | 38 | 690 | 870 | 1.26 | 21 |

Figure 7: Typical technological values, describing powder flowability, shown for milled and sieved MEGGLE lactose grades.



Figures 8 and 9: Sieved lactose grades PrismaLac[®] 40, CapsuLac[®] 60, Sachelac[®] 80, and Spherolac[®] 100 show significant volume flow through apertures with small diameter, as expressed by flowability index. Milled lactose grades, using GranuLac[®] 70 as an example, provides poor flowability, indicated by a high flowability index.

Specific surface

Differences in morphology of milled and sieved grades are reflected by their specific surface area. Milled grades show consistently higher surface area values than coarser sieved grades and are therefore, more prone to inter-particle interaction (figure 10).

| Specific surface area determination by BET | |
|--|---------------------|
| Milled/sieved lactose | (m ² /g) |
| Milled | |
| GranuLac [®] 70 | 0.26 |
| GranuLac [®] 80 | 0.50 |
| GranuLac [®] 140 | 0.42 |
| GranuLac [®] 200 | 0.75 |
| GranuLac [®] 230 | 0.89 |
| SorboLac [®] 400 | 2.10 |
| Sieved | |
| PrismaLac [®] 40 | 0.20 |
| CapsuLac [®] 60 | 0.13 |
| Sachelac [®] 80 | 0.13 |
| Spherolac [®] 100 | 0.22 |

Figure 10: Typical specific surface areas of various milled and sieved MEGGLE lactose grades. BET surface area and pore volume measurement instrument Quantachrome Autosorb-3, adsorbent Kr₂ outgas time and temperature: 7 hrs at 50 °C, in vacuo.

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 11 provides an overview about packaging size and material, and product shelf life.

| Packaging and shelf life | | | |
|----------------------------|-------|--|------------|
| Milled/sieved lactose | | | |
| | Size | Material | Shelf life |
| Milled | | | |
| GranuLac [®] 70 | 25 kg | Paper bag with PE-EVOH-PE inliner | 36 Months |
| GranuLac [®] 80 | | | |
| GranuLac [®] 140 | | | |
| GranuLac [®] 200 | | | |
| GranuLac [®] 230 | | | 24 Months |
| SorboLac [®] 400 | 20 kg | Paper bag with an aluminum-laminated inliner | 36 Months |
| Sieved | | | |
| PrismaLac [®] 40 | 20 kg | Paper bag with PE-EVOH-PE inliner | 36 Months |
| CapsuLac [®] 60 | | | |
| Sachelac [®] 80 | | | |
| Spherolac [®] 100 | | | |

Figure 11: Packaging and shelf life of MEGGLE's milled and sieved lactose grades.



Literature

- [1] Armstrong, N. A. (2007) Tablet manufacture. Encyclopedia of Pharmaceutical Technology, Ed. Swarbrick J., informa healthcare, New York, London: 3653.
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- [3] Von Behren, D. A. (1996) Physical characterization of excipients in practice. Pharm. Technol. 06: 87.
- [4] FlowRatex® Instruction Manual (2010) 28452 Constellation Road, Valencia, Ca. USA.

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