MILLED AND SIEVED LACTOSE

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

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

Technical brochure
Milled and sieved lactose

MEGGLE
EXCIPIENTS & TECHNOLOGY

MEGGLE 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 compactability [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® 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-pharma.com.

MEGGLE offers a broad portfolio of lactose grades meeting pharmaceutical standards with several being dual sourced. Our pharma-dedicated production facility in Wasserburg, Germany is certified according to DIN ISO 9001 : 2008, has implemented cGMP according to the Joint IPEC-PQG Good Manufacturing Practices Guide for Pharmaceutical Excipients and USP General Information Chapter <1078>. It demonstrates the complete range of production capabilities as sieving, milling, agglomeration, spray-drying and co-processing. The US site in Le Sueur/MN produces to equivalent quality standards, as well as provides the same documentation. Furthermore MEGGLE is a member of IPEC (International Pharmaceutical Excipients Council).

MEGGLE invests considerably in raw material resource sustainability, production standards, efficiency and is actively engaged in environmental protection. Lactose meeting pharmaceutical standards is our first priority.

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	Capsule	Tablet			Powder blend	Others		
	Capsule filling	Direct compression	Dry granulation	Wet granulation	Blends, premixes, sachets, triturations	Enhancement of flavours	Media for fermentation	Extrusion-spheronization
Milled	–	–	+	+	+	+	+	+
Sieved	+	–	–	–	+	–	–	–

+ = Highly appropriate – = Poor performance/not recommended

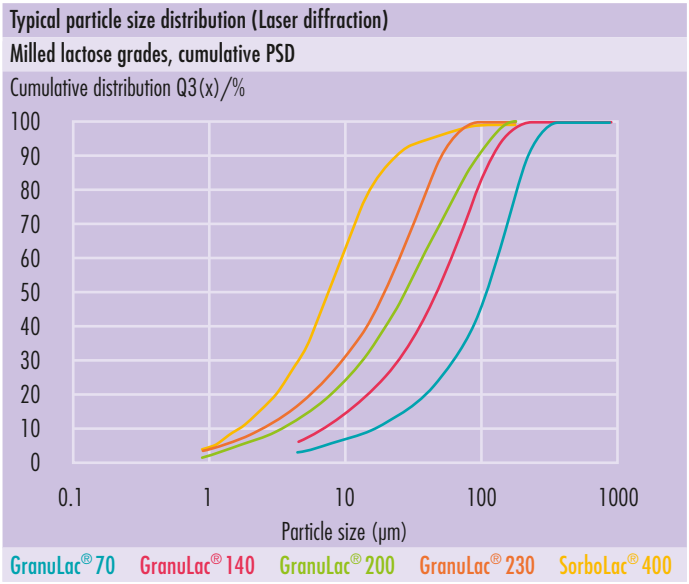
BENEFITS

Milled	Sieved
– Good compactability – Narrow particle size distribution – Good blending properties – High storage stability – High batch-to-batch consistency	– 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.



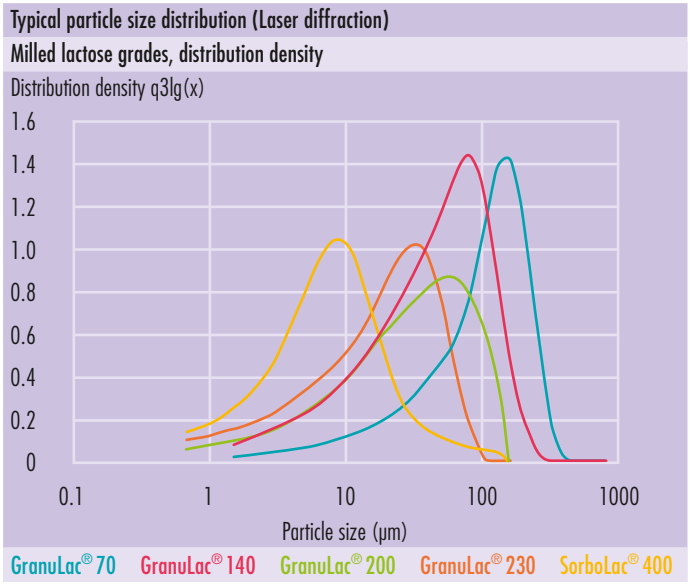
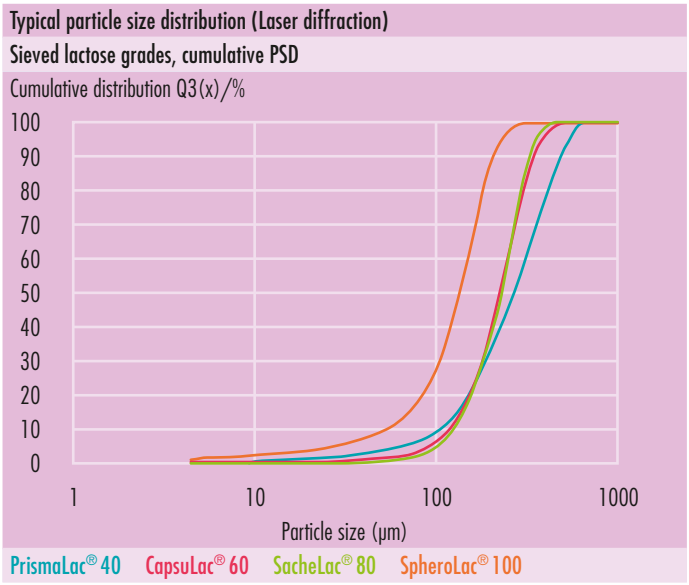


Figure 1: Typical cumulative PSD and distribution density of MEGGLE's milled lactose grades GranuLac® 70, 140, 200, 230 and SorboLac® 400. Analyzed by Sympatec®/Helos & Rodos particle size analyzer.



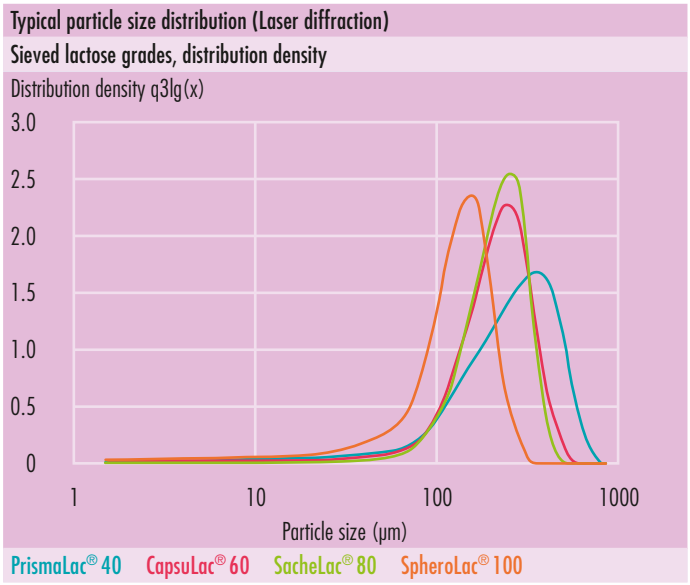


Figure 2: Typical cumulative PSD and distribution density of MEGGLE's sieved lactose grades PrismaLac® 40, CapsuLac® 60, SacheLac® 80 and SpheroLac® 100. Analyzed by Sympatec®/Helos & Rodos particle size analyzer.

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

Sieve data – sieved lactose (German-origin)					
	Lactose type	PrismaLac® 40	CapsuLac® 60	SacheLac® 80	SpheroLac® 100
		specified/typical	specified/typical	specified/typical	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-pharma.com

Isotherms

MEGGLE's milled and sieved alpha-lactose monohydrate products do not adsorb significant amounts of water below 20 °C/80 % relative humidity. **Figure 5** shows sorption and desorption isotherm for GranuLac® 200.

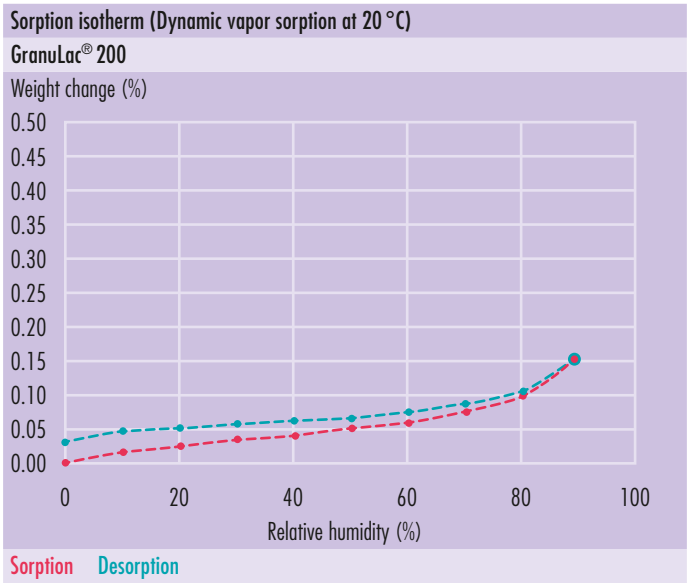


Figure 5: Sorption-desorption isotherm of alpha-lactose monohydrate, using GranuLac® 200 as an example.

Scanning electron micrograph (SEM)

Milled and sieved lactose grades show different morphology. Where sieved products are mainly defined by coarse tomahawk-shaped monocrystals 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)**.

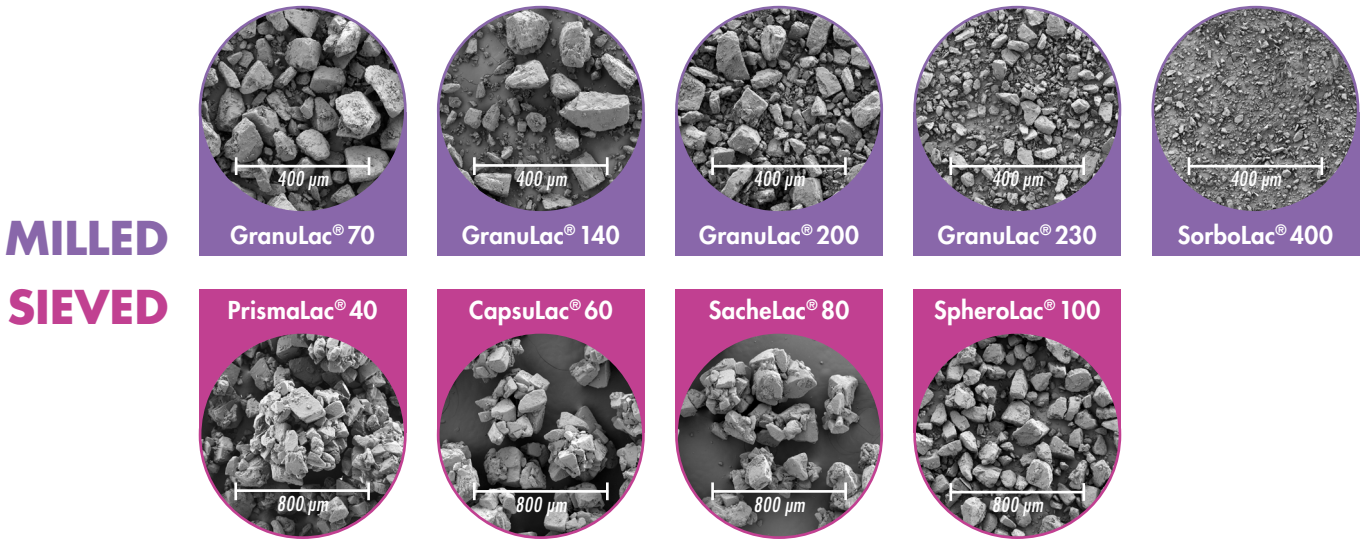


Figure 6: SEM images of various milled and sieved MEGGLE lactose grades.

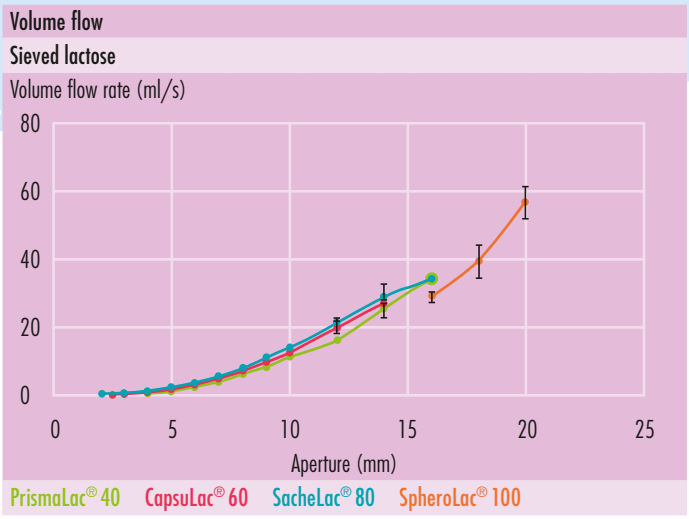
Functional related characteristics

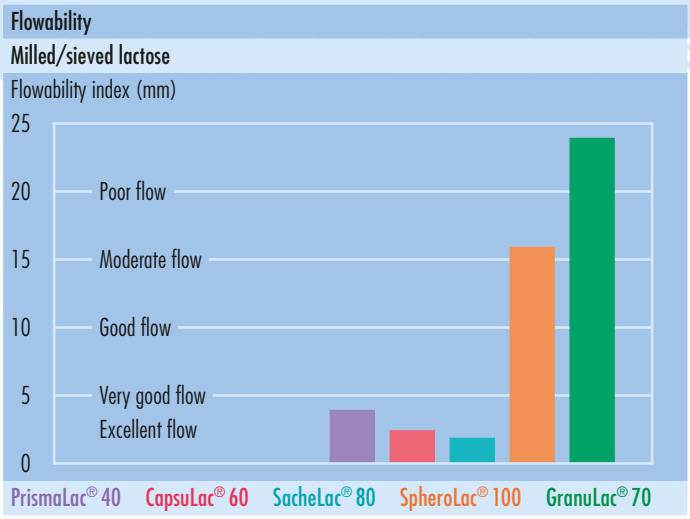
Powder flow

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 (%)
Milled					
GranuLac® 70	43	710	910	1.28	21.98
GranuLac® 140	52	630	890	1.41	29.21
GranuLac® 200	55	530	820	1.55	35.37
GranuLac® 230	56	460	760	1.65	39.47
SorboLac® 400	52	330	590	1.79	44.07
Sieved					
PrismaLac® 40	34	440	540	1.23	18.52
CapsuLac® 60	33	570	700	1.23	18.57
SacheLac® 80	32	570	710	1.25	19.72
SpheroLac® 100	38	690	870	1.26	20.69

Figure 7: Typical powder technological flowability values 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 FI. Milled lactose grades, using GranuLac® 70 as an example, provides poor flowability, indicated by a high flowability index FI.*

Specific surface area

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-particular interaction **(Figure 10)**.

Specific surface area determination by BET
Milled/sieved lactose

	(m^2/g)
Milled	
GranuLac® 70	0.26
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 Kr_2, 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® 140			
GranuLac® 200			
GranuLac® 230			
SorboLac® 400	20 kg	Paper bag with an aluminium-laminated inliner	
Sieved			
PrismaLac® 40	20 kg	Paper bag with PE-EVOH-PE inliner	36 months
CapsuLac® 60	25 kg		
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

[2] Vormans, H., De Boer, A. H., Bolhuis, G. K., Lerk, C. F., Kussendrager K. D., and Bosch, H. (1985) Pharm. Weekblad Sci. 7: 186

[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.

MEGGLE App:

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