



An die interessierte Partei / To whom it may concern

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Quality Unit / Regulatory Affairs

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Doc.-No. EIP-1035-A
Revision 9

Elemental impurities

Ph. Eur. General Text 5.20; USP-NF General Chapter <232> and <233>; ICH Guideline Q3D

Meggle products:

- Lactose Monohydrate Ph. Eur. / USP-NF / JP: CapsuLac[®] 60, FlowLac[®] 90, FlowLac[®] 100, GranuLac[®] 70, GranuLac[®] 140, GranuLac[®] 200, GranuLac[®] 230, PrismaLac[®] 40, SacheLac[®] 80, SorboLac[®] 400, SpheroLac[®] 100, Tablettose[®] 70, Tablettose[®] 80, Tablettose[®] 100

In the production process of the above mentioned products, the elements classified in Class 1, 2A, 2B and 3 are not intentionally added in form of metal catalysts, metal reagents etc.

Permitted concentrations limits were calculated using the Permitted Daily Exposures and assuming a daily intake of the excipients of 10 g (ICH Q3D, No 7 Option 1, stated in table A.2.2). Acceptance levels were defined as 30% of the permitted concentrations.

Testing was conducted for the elements categorised as Class 1, 2A and 3 relevant for oral route of administration according to the ICH Guideline Q3D. Using bracketing principles several representative lots of the products were tested using ICP-MS method in conformance to USP-NF <233>. Testing method has been validated for the matrix of the products.

Representative results are shown for GranuLac[®] 200 on the table below. All results are far below 30% of the acceptance levels for oral application. In consequence, additional controls are not required.

MEGGLE has implemented an ongoing monitoring program for elemental impurities in accordance to the regime of the initial study performed.

Freundliche Grüße / Best regards


Dr. Stefan Dreiheller



Elemental impurities – Summary Results

Ph. Eur. General Text 5.20; USP-NF General Chapter <232> and <233>; ICH Guideline Q3D

Material Name Lactose Monohydrate
 Manufacturer Molkerei MEGGLE Wasserburg GmbH & Co. KG Megglestr. 6 – 12, 83512 Wasserburg, Germany
 Source/Type of Excipient Animal derived (Milk of bovine origin).
 Route of administration (RoA) Oral

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Class	Elements	Elements to be considered		Oral PDE µg/g	Perm. Conc. µg/day	Accept. Level µg/g	Representative Results * GranuLac® 200 µg/g	Method	Comments
		Added*	Based on RoA						
1	Cadmium	Cd	No Yes	0.5	5	0.15	< 0.0009	ICP-MS; USP 40 NF35 <233>	7 batches tested. Monitoring installed (1 / year)
1	Lead	Pb	No Yes	0.5	5	0.15	< 0.0006	ICP-MS; USP 40 NF35 <233>	7 batches tested. Monitoring installed (1 / year)
1	Arsenic (inorg.)	As	No Yes	1.5	15	0.45	< 0.0081	ICP-MS; USP 40 NF35 <233>	7 batches tested. Monitoring installed (1 / year)
1	Mercury (inorg.)	Hg	No Yes	3	30	0.9	< 0.0005	ICP-MS; USP 40 NF35 <233>	7 batches tested. Monitoring installed (1 / year)
2A	Cobalt	Co	No Yes	5	50	1.5	0.0007	ICP-MS; USP 40 NF35 <233>	7 batches tested. Monitoring installed (1 / year)
2A	Vanadium	V	No Yes	10	100	3	< 0.0093	ICP-MS; USP 40 NF35 <233>	7 batches tested. Monitoring installed (1 / year)
2A	Nickel	Ni	No Yes	20	200	6	< 0.0084	ICP-MS; USP 40 NF35 <233>	7 batches tested. Monitoring installed (1 / year)
2B	Thallium	Tl	No No	n/a					
2B	Gold	Au	No No	n/a					
2B	Palladium	Pd	No No	n/a					
2B	Iridium	Ir	No No	n/a					
2B	Osmium	Os	No No	n/a					
2B	Rhodium	Rh	No No	n/a					
2B	Ruthenium	Ru	No No	n/a					
2A	Selenium	Se	No No	n/a					
2B	Silver	Ag	No No	n/a					
2B	Platinum	Pt	No No	n/a					
3	Lithium	Li	No No	n/a					
3	Antimony	Sb	No No	n/a					
3	Barium	Ba	No No	n/a					
3	Molybdenum	Mo	No No	n/a					
3	Copper	Cu	No No	n/a					
3	Tin	Sn	No No	n/a					
3	Chromium	Cr	No No	n/a					

* "< X" implies values are below LoQ (limit of quantification) which is X

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