



To whom it may concern

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Quality Unit

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Doc.-No. EIP-1035 -A  
Revision 17

## Elemental Impurities

**Ph. Eur. General Text 5.20; USP-NF General Chapter <232> and <233>; ICH Guideline Q3D(R2)**

MEGGLE Products:

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

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(R2), 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 and 2A relevant for oral route of administration according to the ICH Guideline Q3D(R2). 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 on the table below which are valid for all mentioned MEGGLE products. 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.

Best regards

**MEGGLE GmbH & Co. KG**

**Dr. Stefan Dreiheller**

Regulatory Affairs / Specification Management



## Elemental impurities – Summary Results

Ph. Eur. General Text 5.20; USP-NF General Chapter <232> and <233>; ICH Guideline Q3D(R2)

Material Name Lactose Monohydrate  
 Manufacturer MEGGLE GmbH & Co. KG Megglestr. 6 – 12, 83512 Wasserburg am Inn, 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/day	Perm. Conc. µg/g	Accept. Level µg/g	Representative Results *	Method	Comments	
		Added	Based on RoA							
1	Cadmium	Cd	No	Yes	5	0.5	0.15	< 0.0009	ICP-MS; USP 40 NF35 <233>	7 batches tested. Monitoring installed (1 / year)
1	Lead	Pb	No	Yes	5	0.5	0.15	< 0.0006	ICP-MS; USP 40 NF35 <233>	7 batches tested. Monitoring installed (1 / year)
1	Arsenic (inorg.)	As	No	Yes	15	1.5	0.45	< 0.0081	ICP-MS; USP 40 NF35 <233>	7 batches tested. Monitoring installed (1 / year)
1	Mercury (inorg.)	Hg	No	Yes	30	3	0.9	< 0.0005	ICP-MS; USP 40 NF35 <233>	7 batches tested. Monitoring installed (1 / year)
2A	Cobalt	Co	No	Yes	50	5	1.5	0.0007	ICP-MS; USP 40 NF35 <233>	7 batches tested. Monitoring installed (1 / year)
2A	Vanadium	V	No	Yes	100	10	3	< 0.0093	ICP-MS; USP 40 NF35 <233>	7 batches tested. Monitoring installed (1 / year)
2A	Nickel	Ni	No	Yes	200	20	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					
2B	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