Elemental Impurities

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

MEGGLE Product:

Co-processed Excipient: RetaLac®

The MEGGLE Product is a co-processed, directly compressible spray agglomerate containing
- 50 % Lactose Monohydrate (Ph. Eur. / USP-NF / JP),
- 50 % Hypromellose (Ph. Eur. / USP-NF / JP).

In the production process of the above mentioned product, 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). Several representative lots of the product were tested using ICP-MS method in conformance to USP-NF ⟨233⟩. Testing method has been validated for the matrix of the products.

Results are shown for the product on the table below. All results are 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.

Elemental impurities – Summary Results

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

Material Name: RetaLac®
Subcontracted Production Site: IPC Process Center GmbH & Co. KG, Grunaer Weg 26, 01277 Dresden, Germany
Release Site: MEGGLE GmbH & Co. KG, Megglestr. 6-12, 83512 Wasserburg am Inn, Germany
Source/Type of Excipient: Lactose: Animal derived (Milk of bovine origin); Hypromellose: Synthetic from cellulose
Route of administration (RoA): Oral

Class	Elements		Elements to be considered		Oral PDE	Perm. Conc.	Accept. Level	Results*	Method	Comments
			Added	Based on RoA	µg/day	µg/g	µg/g	µg/g		
1	Cadmium	Cd	No	Yes	5	0.5	0.15	< 0.15	ICP-MS; USP-NF⟨233⟩	7 batches tested. Monitoring installed (1 / year)
1	Lead	Pb	No	Yes	5	0.5	0.15	< 0.15	ICP-MS; USP-NF⟨233⟩	7 batches tested. Monitoring installed (1 / year)
1	Arsenic (inorg.)	As	No	Yes	15	1.5	0.45	< 0.15	ICP-MS; USP-NF⟨233⟩	7 batches tested. Monitoring installed (1 / year)
1	Mercury (inorg.)	Hg	No	Yes	30	3	0.9	< 0.15	ICP-MS; USP-NF⟨233⟩	7 batches tested. Monitoring installed (1 / year)
2A	Cobalt	Co	No	Yes	50	5	1.5	< 0.15	ICP-MS; USP-NF⟨233⟩	7 batches tested. Monitoring installed (1 / year)
2A	Vanadium	V	No	Yes	100	10	3	< 0.15	ICP-MS; USP-NF⟨233⟩	7 batches tested. Monitoring installed (1 / year)
2A	Nickel	Ni	No	Yes	200	20	6	< 1	ICP-MS; USP-NF⟨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": < **LoQ** (Limit of Quantification)

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