Elemental Impurities

Inhalation Lactose (EU)

Product group: Inhalation
Brand name: Lactohale®
Product description: Lactose Anhydrous

Dear Customer,

In the framework of the ICH Q3D guideline, DFE Pharma tested batches of pharmaceutical grade lactose, originating from the production site located in Borculo, The Netherlands (Europe) representing the brand name mentioned above.
The raw material used for the production of Lactohale® 400 is an anhydrous lactose grade which is produced at our production site in Nörten-Hardenberg, Germany. The final modification of the raw material performed at our production site in Borculo, The Netherlands does not add any elemental impurities to the product as we know from our other Lactohale® grades produced at the same facility; please see PD-0617 for reference. Representative data is shown for the raw material in the chart below. Neither the elements listed below, nor elements classified as 2B, are intentionally added during the production process. Therefore DFE Pharma performed analysis on relevant elemental impurities categorized as 1, 2A and class 3 elements by the ICH Q3D guideline. Analysis was performed using the analysis technique ICP-MS (Inductively Coupled Plasma-Mass Spectrometry) conform USP-NF <233>.

Metal	Class	Limit*1 (ppm)	Lactose Anhydrous*2 Batch 100H69M
Arsenic	1	0.2	<0.01
Cadmium	1	0.2	<0.005
Mercury	1	0.1	<0.003
Lead	1	0.5	<0.02
Cobalt	2A	0.3	<0.005
Nickel	2A	0.5	<0.03
Vanadium	2A	0.1	<0.002
Molybdenum	3	1	0.04
Chromium	3	0.3	<0.03
Antimony	3	2	<0.005
Tin	3	6	<0.01
Lithium	3	2.5	<0.004
Barium	3	30	0.008
Copper	3	3	<0.01

*1: Limits are based on option 1 of the ICH Q3D guidelines, based on administration of not more than 10g of drug product per day (stated in table A.2.2).
*2: "<X" implies values are below detection limit X.

DFE Pharma GmbH & Co. KG
Kleyer Strasse 187, 47574 Goch, Germany, P.O. Box 20 21 20, 47568 Goch, Germany, T. +49 2823 9288 770, F. +49 2823 9288 7799

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Values for all analyzed batches of Lactohale® produced at our production site located in Borculo, The Netherlands and the raw material (anhydrous lactose grade) originating from our production site in Nörten-Hardenberg, Germany were below 30% of the limits mentioned in the table above.

A risk assessment was performed. This document is available for review during audits. Conclusion of the risk assessment is that all values obtained are below 30% of the limits and thus do not need additional control, the change control procedure is the key to maintain this situation. The levels of ICH Q3D relevant elemental impurities are monitored on regular basis.

This statement substitutes all previous versions issued for the brand names mentioned above.
We trust this information, which is made up to the best of our knowledge, will be helpful to you.

Name : Armand M. Janssen
Job title : QA Regulatory Affairs Officer
Signature :

This document is controlled by a validated, electronic system and is valid without signature.
The above facsimile signature is only for display.

DFE Pharma GmbH & Co. KG
Kleyer Strasse 187, 47574 Goch, Germany, P.O. Box 20 21 20, 47568 Goch, Germany, T. +49 2823 9288 770, F. +49 2823 9288 7799