



浙江海洲制药有限公司

Zhejiang Haizhou Pharmaceutical Co., Ltd.

Zhejiang Haizhou Pharmaceutical Co., Ltd.

Yantai Industrial Zone,

Linhai City, Zhejiang 317016,

China

May 2, 2018

Product: **Methocarbamol**

Statement

To whom it may concern,

With regard to ICH Q3D Guideline for Elemental Impurities, We, Zhejiang Haizhou Pharmaceutical Co., Ltd., hereby state that no element listed as below is intentionally added in the manufacturing process of the product Methocarbamol.

Elements concerned in ICH Q3D:

Class 1: Cd, Pb, As, Hg;

Class 2A: Co, V, Ni;

Class 2B: Tl, Au, Pd, Ir, Os, Rh, Ru, Se, Ag, Pt;

Class 3: Li, Sb, Ba, Mo, Cu, Sn, Cr.

As described in ICH Q3D, "Class 2B elements have a reduced probability of occurrence in the drug product related to their low abundance and low potential to be co-isolated with other materials. As a result, they may be excluded from the risk assessment unless they are intentionally added during the manufacture of drug substance, excipients or other components of the drug product." "Class 3: For oral routes of administration, unless these elements are intentionally added, they do not need to be considered during the risk assessment."

Hence, we tested three consecutive batches of Methocarbamol only for Class 1 and 2A by ICP-MS. The results of analysis are given in table 1 and risk assessment is showed in table 2.

Table 1: Analysis Results of Methocarbamol

EIs	Class	Batch number (µg/kg)		
		18ME03001	18ME03002	18ME03003
Cd	1	<4.53	<4.53	<4.53
Pb	1	<12.97	<12.97	<12.97
As	1	<34.51	<34.51	<34.51
Hg	1	<14.80	<14.80	<14.80
Co	2A	<1.54	<1.54	<1.54
V	2A	<95.56	<95.56	<95.56
Ni	2A	<22.18	<22.18	<22.18

Table 2: Risk assessment table for Methocarbamol

Els	Class	Source Added during process.	Source Manufacturing equipment	Source container	Option 1 Permitted Conc ug/g	Total elemental impurity contribution (µg/kg)	Control threshold (µg/g)	Action
Cd	1	No	No	No	0.5	<4.53	0.15	No further controls required
Pb	1	No	No	No	0.5	<12.97	0.15	No further controls required
As	1	No	No	No	1.5	<34.51	0.45	No further controls required
Hg	1	No	No	No	3.0	<14.80	0.9	No further controls required
Co	2A	No	No	No	5.0	<1.54	1.5	No further controls required
V	2A	No	No	No	10.0	<95.56	3	No further controls required
Ni	2A	No	No	No	20.0	<22.18	6	No further controls required

Zhejiang Haizhou Pharmaceuticals Co., Ltd herewith confirms that if the observed contents of respective elemental impurities are less than 30% of the ICH Q3D option 1 limit for products used orally then the respective potential elemental impurity is considered as absent and no further controls are required.

Sincerely,



Ms. Peng Wenjun

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