



8-Hydroxyquinoline

Comments on the proposed classification and labelling according to the CLH report

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04.11.2014

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Comments on the proposed classification and labelling according to the CLH report (Version number: 3 Date: September 2014)

1) Acute oral toxicity

Classification is based on a mouse study (Dickhaus & Heisler, 1981b) LD₅₀ 177 mg/kg bw) with mortalities occurring within 24 h after administration. However the test item was not specified in that study.

This low LD₅₀ is not supported by studies in mice with specified test item purity:

In an "*In vivo spermatogonial chromosome aberration study*" (August, 2007) no mortalities were observed at dose levels up to 300 mg/kg bw 8-Hydroxyquinoline in mice.

Also in repeated dose studies (NTP, 1985) no mortalities occurred at dose levels of up to 12000 ppm 8-Hydroxyquinoline in feed (~ 2400 mg/kg bw/d) in at 15-day study in mice and no mortalities were observed at dose levels up to 6000 ppm 8-Hydroxyquinoline in feed administered for 90-days in mice (corresponding to 774/888 mg/kg bw/d), the highest dose tested.

Considering the weight of evidence the observation of the LD₅₀ in mice as reported in the Dickhaus & Heisler (1981b) study is considered spurious and may be due to impurities in the test item, as no specification or analysis was provided.

A more reasonable but conservative classification is proposed:

Acute Tox 4 H302, Harmful if swallowed

2) Reproductive toxicity

We agree with non-classification for reproductive toxicity regarding sexual function and fertility.

We disagree with the proposed classification for developmental toxicity based on findings in a rabbit developmental study (Fascineli, 2006):

8-Hydroxyquinoline was administered at 0, 5, 15 and 60 mg/kg to groups of pregnant New Zealand White rabbits. The administration of 8-Hydroxyquinoline at 15 and 60 mg/kg to pregnant rabbits produced several cases of transient nervous excitation followed by lethargy after the administration of 8-Hydroxyquinoline. No malformations were noted upon visceral, head (soft tissue) or skeletal examination. However, upon external examination slightly increased incidences of omphalocele were noted at 15 and 60 mg/kg bw/d affecting 3 or 4 litters, respectively.

However, in a developmental toxicity study, Copper 8-hydroxyquinolate was administered to pregnant New Zealand White rabbits by gavage at dose levels of 0, 7, 15, or 30 mg/kg/day from days 7 through 19 of gestation. There was no evidence of developmental toxicity in this study (US EPA, 2010).

It is thus concluded that bolus administration of 8-Hydroxyquinoline, which is potent metal ion chelating agent, scavenges efficiently essential metal ions causing a deficiency in these micronutrients. Subsequently, the prenatal development is adversely affected by this deficiency as a secondary effect.

The increased incidence of omphalocele and also a transient nervous excitation is limited to administration by gavage of 8-Hydroxyquinoline and is not occurring after oral exposure via the diet nor by the administration of Copper-8-hydroxyquinoline chelate complex. It is concluded that this effect, this mechanism of action, is not relevant to humans.

A classification of 8-Hydroxyquinoline for developmental toxicity is not warranted.



References:

Author(s)	Year	Title Testing Facility Owner / Source (where different from owner) Report No GLP or GEP status (where relevant) Published or not
August M.	2007	in vivo Mammalian Spermatogonial chromosome aberration test of 8-Hydroxyquinoline in NMRI mouse by oral administration LPT Lab. of Pharm. and Tox. GmbH & Co. KG, Hamburg, Germany Probelte S.A. Report-no. 19589/05 GLP: yes Published: no
Dickhaus, S., Heisler, E.	1981b	Akute Toxizitätsprüfung von der Substanz ' Hydroxychinolin' nach peroraler Applikation an der Maus (English translation amended) Pharmatox GmbH, Sehnde, Germany Probelte S.A. Report-no. 1-1-80-81 GLP/GEP: no Published: no
Fascineli, M.L.	2006	Prenatal Developmental Toxicity Study in New Zealand White Rabbits for 8-Hydroxyquinoline BIOAGRI Laboratórios, Planaltina/DF - 73301-970 - Brazil Probelte S.A. Report-no. RF-3154.315.009.04 GLP: yes Published: no
NTP National Toxicology Program	1985	Toxicology and carcinogenesis studies of 8-hydroxyquinoline (CAS No. 148-24-3) in F344/N rats and B6C3F1 mice (feed studies) National Institute of Health, USA US NTIS PB 85-213361, springfield, VA., 1-170 Report-no. NTP TR 276 GLP/GEP: no Published: yes
US EPA	2010	Copper 8-quinolinolate. Human Health Effects Scoping Document for the Registration Review Decision. EPA-HQ-OPP-2010-0454-0002