European Food Safety Authority

Scientific Statement of the Panel on food additives, flavourings, processing aids and materials in contact with food on a request from the Commission related to

an update on the hazard assessment of 2-isopropyl thioxanthone (ITX) in food contact materials

Question number EFSA-Q-2007-088

Adopted on 25 September 2007

The Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food has been asked by the European Commission to review its previous opinion on 2-isopropyl thioxanthone (ITX), adopted on 7 December 2005 (available at: http://www.efsa.europa.eu/en/science/afc/afc_opinions/1256.html), in the light of the results of a 28-day repeated-dose oral toxicity study on ITX, submitted by industry in January 2007. At the time of the 2005 opinion, only studies on genotoxicity, showing the absence of genotoxicity *in vivo*, were available and no further comment on the safety of ITX could be made due to the lack of other toxicity data.

The new 28-day study (NOTOX, 2006) was conducted according to the OECD guideline for a repeated dose 28-day oral toxicity study in rodents (OECD, 1995) and was performed under Good Laboratory Practice. ITX was administered to groups of 5 male and 5 female Wistar rats by gavage at daily doses of 0, 50, 150, and 1 000 mg/kg bw/day for 28 consecutive days. Two recovery groups (5 male and 5 female rats/group) received ITX at 0 and 1 000 mg/kg bw/day for 28 days and were sacrificed 2 weeks after the end of the 28-day administration period. The study protocol included daily cage side observation for clinical signs, weekly assessment of body weight gain and food consumption and a functional observation test. Clinical pathology, clinical chemistry in blood, haematology and organ weight determinations were performed at termination.

In the main study groups sacrificed at the end of the 28-day administration of ITX, dose-dependent increases in total serum protein, serum albumin and serum cholesterol, accompanied by increased absolute and relative liver weights, were observed in both male and female animals. These increases were statistically significant already at the lowest dose level of 50 mg ITX/kg bw/day, but were not accompanied by histopathological changes in the liver. At the two higher ITX doses (150 and 1 000 mg/kg bw/day), minimal to slight centrilobular hypertrophy was observed in both male and female rats. The

incidence of centrilobular hypertrophy showed dose-related increases in the 150 and 1 000 mg/kg bw/day groups (no statistical evaluation available from the report).

In addition to the effects of ITX on the liver, minimal to slight squamous hyperplasia of the forestomach was observed in males and females receiving 1000 mg ITX/kg bw/day. Diffuse follicular hyperplasia of the thyroid, described as minimal to slight, was also noted at 1000 mg ITX/kg bw/day. In addition, a dose-dependent increase in hyaline droplets in the kidney, accompanied by tubular basophilia at the corticomedullary junction of the kidney was observed in male rats. Kidney tubular basophilia also occurred at a low incidence in high-dose female rats. All histopathological changes, except tubular basophilia in the kidney in male rats, were described as being reversible and were no longer present in the animals sacrificed two weeks after the end of administration of a dose of 1000 mg ITX/kg bw/day.

Due to the short duration of the study, only limited conclusions can be drawn. The Panel considers the increased absolute and relative liver weights and the renal tubular basophilia observed at the lowest dose studied (in males) as potentially relevant effects for an assessment of ITX. Effects on both liver and kidney were dose-dependent and the liver effects were also accompanied by dose-dependent changes in clinical chemistry.

Bearing in mind the Panel's previous opinion that the existing *in vivo* genotoxicity studies do not indicate a genotoxic potential for ITX, an assessment of potential health risks in relation to the possible presence of ITX in food would require additional data on ITX effects after longer term administration.

KEY WORDS

2-Isopropyl thioxanthone (ITX), CAS 5495-84-1; photoinitiators; inks; food contact materials, genotoxicity; 28-day study, toxicology

DOCUMENTS PROVIDED TO THE EFSA

NOTOX B.V (2006) Report on Repeated-dose 28-day oral toxicity study with 2-isopropylthioxanthone by daily gavage in the rat followed by a 14-day recovery period, NOTOX Project 463736, 21. November 2006.

REFERENCES

EFSA (European Food Safety Authority), 2005, opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food on 2-Isopropyl thioxanthone (ITX) and 2-ethylhexyl-4-dimethylaminobenzoate (EHDAB) in food contact materials, adopted on 7 December 2005. The EFSA Journal 293, 1-19 (2005): http://www.efsa.europa.eu/en/science/afc/afc_opinions/1256.html

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SCIENTIFIC PANEL MEMBERS

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* A member of the Panel declared an interest and therefore he did not participate in the discussion. Details on the declarations of interest can be found in the minutes of the Panel meeting at: http://www.efsa.europa.eu/EFSA/ScientificPanels/AFC/efsa_locale-1178620753812_Meetings424.htm