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Scientific Committee on Food **SCF/CS/CNTM/MYC/28 Final**

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Updated opinion of the Scientific Committee on Food on Fumonisin B1, B2 and B3

(expressed on 4 April 2003)

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http://europa.eu.int/comm/food/fs/sc/scf/index_en.html

TERMS OF REFERENCE

The Scientific Committee is requested to consider if the TDI of 2 microgram/kg bw for fumonisin B_1 established in its opinion of 17 October 2000 can be considered as a group TDI applicable to fumonisin B_1, fumonisin B_2 and fumonisin B_3, alone or in combination.

BACKGROUND

The Scientific Committee on Food expressed an opinion on fumonisin B_1 (FB_1) on 17 October 2000 (SCF, 2000). The Committee concluded that there is no adequate evidence that FB_1 is genotoxic and that information on the mode of action justifies a threshold approach. The Committee also took into account the approximate NOAEL in horses of 0.2 mg FB_1/kg bw/day. The Committee considered equine leukoencephalomalacia (ELEM) in horses as a severe effect, which does not need long-term exposure to reach fatal expression, and would expect that this effect if induced in humans, would be observed after short-term exposure. Therefore, the Committee concluded that there was no need for an additional uncertainty factor and allocated to fumonisin B_1, on the basis of the overall NOAEL from subchronic toxicity study in rats and the long-term toxicity/carcinogenicity study in rats equivalent to 0.2 and 0.25 mg/kg bw/day, respectively, a TDI of 2 microgram/kg bw, using a safety factor of 100. The Committee also considered recent indications that cardiovascular toxic effects of FB_1 could play a role in the development of other toxic effects observed.

The Joint FAO/WHO Expert Committee on Food Additives (JECFA) evaluated fumonisin B_1, fumonisin B_2 and fumonisin B_3 at its fifty-sixth meeting (WHO Technical Report Series, 2002). The JECFA focused its evaluation on toxicological studies of fumonisin B_1 and on studies of intake of contaminated maize and maize products, as most biological data were available on fumonisin B_1, and maize is the major source of intake. The JECFA stated that in many studies culture materials and naturally contaminated maize were used, which contain besides fumonisin B_1 several other fumonisins primarily fumonisin B_2 and B_3. The JECFA stated furthermore that the toxicological profile of fumonisin B_2 and fumonisin B_3 are very similar to that of fumonisin B_1. The JECFA concluded that the pivotal studies that could serve as the basis for a tolerable daily intake of fumonisin B_1 were the short term and long-term studies of toxicity in rodents. On the basis of these studies, the overall NOEL for renal toxicity was 0.2 mg/kg bw/day. The JECFA allocated a group provisional maximum tolerable daily intake (PMTDI) of 2 microgram/kg of body weight to fumonisins B_1, B_2, and B_3, alone or in combination, on the basis of the NOEL of 0.2 mg/kg body weight per day and a safety factor of 100.

OPINION

The Committee considered the following information as evaluated by JECFA (WHO Technical Report Series, 2002):

1) Fumonisins are mycotoxins produced by fungi of the genus *Fusarium*. Fumonisin B_1 is the diester of propane-1,2,3-tricarboxylic acid and 2S-amino-12S,16R-dimethyl-3S,5R,10R,14S,15R-pentahydroxyeicosane in which the C-14 and C-15 hydroxy groups are esterified with terminal carboxy group of propane-1,2,3-tricarboxylic acid. Fumonisin B_2 is the C-10 deoxy analogue of fumonisin B_1 in which the corresponding stereogenic units of the eicosane backbone possess the same configuration. The full stereochemical structure of fumonisin B_3 is unknown, although the amino-terminal end of fumonisin B_3 has the same absolute configuration as that of fumonisin B_1 (WHO Technical Report Series, 2002).

2) As most biological data were available on fumonisin B_1 the Committee had focused in 2000 its evaluation on the toxicological studies of fumonisin B_1. However, the toxicological profiles of fumonisin B_2 and B_3, as far as the toxicity data are available, are very similar to that of fumonisin B_1. Various chemical derivatives of fumonisins have been tested in a number of biological test systems to gain insight into structure-activity relationship. The free amino group appears to play a specific role in the biological activity of fumonisin B_1 (WHO Technical Report Series, 2002).

The Committee also considered the results of a comparative study of the fumonisins B_1, B_2 and B_3 with respect to their relative cytotoxicity to primary rat hepatocytes and their potential to induce hepatocyte nodules in an initiation/promotion model using male Fischer rats. Cytotoxicity as measured by lactate dehydrogenase release was highest in fumonisin B_2, followed by fumonisin B_3 and fumonisin B_1. All 3 fumonisins were able to induce hepatocyte nodules when fed at dietary concentrations of 500 or 1000 mg/kg over 21 days to the rats (Gelderblom *et al.*,1993).

Furthermore, almost equal cytotoxicity was found for the fumonisins B_1 and B_2 when tested in 7 different rat hepatoma cell lines and in one dog kidney cell line (Shier *et al.*, 1991).

The Committee also noted that in primary rat hepatocytes, fumonisin B_2 was as effective as fumonisin B_1 in inhibiting the *de novo* biosynthesis of sphingolipids (*Wang et al.,* 1991; Norred *et al.,* 1992). In ponies of varying age and gender, feed containing 75 mg/kg fumonisin B_2 or B_3 (equivalent to 0.75 mg/kg bw), free sphinganine concentrations in liver was increased relative to controls 136 and 27 fold, respectively, and 56 and 11 fold in kidney. The Committee noted that the diet containing fumonisin B_2 contained also 3 mg/kg fumonisin B_1 (Riley, 1997).

CONCLUSION

The Committee concluded on the basis of the above that the TDI for fumonisin B_1 could be expanded by establishing a group TDI of 2 microgram/kg body weight for the total of fumonisin B_1, B_2, and B_3, alone or in combination.

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