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

(expressed on 4 April 2003)
TERMS OF REFERENCE

The Scientific Committee is requested to consider if the TDI of 2 microgram/kg bw for fumonisin B₁ established in its opinion of 17 October 2000 can be considered as a group TDI applicable to fumonisin B₁, fumonisin B₂ and fumonisin B₃, alone or in combination.

BACKGROUND

The Scientific Committee on Food expressed an opinion on fumonisin B₁ (FB₁) on 17 October 2000 (SCF, 2000). The Committee concluded that there is no adequate evidence that FB₁ 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 FB₁/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 B₁, 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 FB₁ could play a role in the development of other toxic effects observed.

The Joint FAO/WHO Expert Committee on Food Additives (JECFA) evaluated fumonisin B₁, fumonisin B₂ and fumonisin B₃ at its fifty-sixth meeting (WHO Technical Report Series, 2002). The JECFA focused its evaluation on toxicological studies of fumonisin B₁ and on studies of intake of contaminated maize and maize products, as most biological data were available on fumonisin B₁, 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 B₁ several other fumonisins primarily fumonisin B₂ and B₃. The JECFA stated furthermore that the toxicological profile of fumonisin B₂ and fumonisin B₃ are very similar to that of fumonisin B₁. The JECFA concluded that the pivotal studies that could serve as the basis for a tolerable daily intake of fumonisin B₁ 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 B₁, B₂, and B₃ 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.
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 B₁ 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 B₂ is the C-10 deoxy analogue of fumonisin B₁ in which the corresponding stereogenic units of the eicosane backbone possess the same configuration. The full stereochemical structure of fumonisin B₃ is unknown, although the amino-terminal end of fumonisin B₃ has the same absolute configuration as that of fumonisin B₁ (WHO Technical Report Series, 2002).

2) As most biological data were available on fumonisin B₁ the Committee had focused in 2000 its evaluation on the toxicological studies of fumonisin B₁. However, the toxicological profiles of fumonisin B₂ and B₃, as far as the toxicity data are available, are very similar to that of fumonisin B₁. 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 B₁ (WHO Technical Report Series, 2002).

The Committee also considered the results of a comparative study of the fumonisins B₁, B₂ and B₃ 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 B₂, followed by fumonisin B₃ and fumonisin B₁. 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 B₁ and B₂ 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 B₂ was as effective as fumonisin B₁ 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 B₂ or B₃ (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 B₂ contained also 3 mg/kg fumonisin B₁ (Riley, 1997).
CONCLUSION

The Committee concluded on the basis of the above that the TDI for fumonisin B₁ could be expanded by establishing a group TDI of 2 microgram/kg body weight for the total of fumonisin B₁, B₂, and B₃, alone or in combination.

REFERENCES


