Toxicity

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24. The toxicity of T-2 and HT-2 has been reviewed by EFSA (2011, 2017b), JECFA (2002, 2016, 2022) and the Scientific Committee on Food (SCF) (2002). All Committees agreed that T-2 and HT-2 had both acute and chronic effects.

25. The primary acute effect of T-2 and HT-2 toxicity is emesis. This effect is dependent on the maximum concentration in plasma (Cmax) and has been observed upon single oral and intraperitoneal exposures to T-2 and HT-2 in mink (Wu et al., 2016). The primary chronic effects of T-2 and HT-2 toxicity are haematotoxicity, immunotoxicity and reduced body weight gain. Exposure to T-2 for up to 12 weeks via the diet resulted in reduced total leucocyte counts in male Wistar rats (Rahman et al., 2014), while exposure for three weeks, also via the diet, resulted in reduced body weight gain in juvenile pigs (Rafai et al., 1995a,b). Both acute and chronic effects were dose-dependent and occurred over a similar

dose range (1.8 – 3.3 µg/kg bodyweight (bw)). The apparent difference in sensitivity to acute or chronic effects arises from different uncertainty factors (UF) which have been applied when deriving the corresponding HBGVs.

26. T-2 and HT-2 also demonstrated dermal toxicity, developmental and reproductive toxicity, and neurotoxicity; however, these effects occurred at higher doses.

Toxicokinetics

27. The toxicokinetics of T-2 and HT-2 have been reviewed previously by JECFA (2001) and EFSA (2017a). Very little information is available concerning the *in vivo* absorption of T-2 and HT-2 in animals after oral administration.

28. Pfeiffer et al. (1988) administered single doses of radiolabelled T-2 at two doses (0.15 and 0.60 mg/kg) to male Sprague-Dawley rats via three routes (oral, intravenous, dermal). Urine and faeces were collected over six days. The results demonstrated that excretion was rapid and largely complete within 72 hours for oral and intravenous routes but slower following dermal exposure. Overall, T-2 was predominantly excreted in faeces, the faeces-to-urine ratio for the toxin and its metabolites being approximately 5:1.

29. In mice and rats (strain not specified), orally administered tritium-labelled T-2 was rapidly eliminated via faeces and urine. In mice, the toxin was rapidly distributed to the liver, kidney and other organs, without accumulating in any organ. In rats, T-2 was excreted via faeces partly as HT-2 toxin, NEO and three unidentified metabolites (Matsumoto et al., 1978). When tritiated T-2 was administered directly into the small intestine of male rats, 40 to 57 % of radioactivity was found in bile and blood, suggesting an extensive hydrolysis to HT-2 and other metabolites during the rapid intestinal absorption of T-2 (Coddington et al., 1989).

30. The metabolism of T-2 and HT-2 in humans and other species is complex and was previously reviewed by EFSA (2011). In brief, phase 1 metabolites arise from either hydrolysis of ester groups, hydroxylation, or de-epoxidation. These reactions may also occur in combination. In 2017, EFSA decided to review relevant new data on T-2 and HT-2 and noted that glucuronides are the most prevalent mammalian phase 2 metabolites of T-2 and HT-2 (EFSA, 2017a). In 2022, EFSA reviewed the toxicokinetics and fate of T-2 and HT-2 in ruminants. The Panel noted that “results of *in vivo* studies with cows point to a rapid absorption, an extensive biotransformation to several less toxic metabolites

and a rapid excretion of the parent compound and its metabolites, with negligible tissue accumulation and transfer to milk” (EFSA, 2022). Therefore, accumulation of T-2 and HT-2 in animal tissues and milk is not expected to occur at a significant level.