Toxicity

In this guide

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22. The toxicity of T-2 and HT-2 has been reviewed previously by EFSA (2011a, 2017c), JECFA (2002, 2016, 2022) and the SCF (2002). All Committees agreed that these trichothecenes had both acute and chronic effects. An acute refence dose (ARfD) is the estimated amount of a substance in food or drink that can be ingested in a single meal or day without appreciable health risk to the consumer. The tolerable daily intake (TDI) is the estimated amount of a substance that can be ingested daily over a lifetime without posing a significant health risk.

23. The primary chronic effects of T-2 and HT-2 toxicity are haematotoxicity, immunotoxicity and reduced body weight gain. The primary acute effect of T-2 and HT-2 toxicity is emesis, where the effect is Cmax-dependent (related to peak concentration). Both acute and chronic effects occur in a similar dose range (1.8 – 3.3 µg/ kg bw), but the perceived difference in sensitivity to acute or chronic effects arises from different uncertainty factors

which have been applied when deriving the corresponding HBGVs.

24. T-2 and HT-2 also demonstrated dermal toxicity, developmental and reproductive toxicity, and neurotoxicity, however these effects occurred at lower concentrations.

Toxicokinetics

25. The toxicokinetics of T-2 and HT-2 have been reviewed previously by JECFA (2001) and EFSA (2017a). In summary, there is very little information on the *in vivo* absorption of T-2 and HT-2 in animals after oral administration. Rapid absorption has been confirmed by the excretion of total radioactivity in rats within 48 hours after oral gavage. T-2 radioactivity was rapidly distributed to the liver, kidney and other organs without accumulation in any organ in orally dosed rats and mice. 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 (EFSA, 2017a).

26. The metabolism of T-2 and HT-2 in humans and other species is complex and was previously reviewed by EFSA (2011a). In brief, phase I 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 new relevant data on T-2 and HT-2 and noted that glucuronides are the most prevalent mammalian phase II metabolites of T-2 and HT-2 (EFSA, 2017a).

27. 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 level of significance.