Risk characterisation - Citrinin

In this guide

70. The available data indicates that CIT is nephrotoxic causing swelling and eventual necrosis of the kidneys. CIT also affects liver function but to a lesser extent. Exposure to CIT has also been associated with reproductive toxicity and teratogenic and embryotoxic effects.

71. EFSA (2012) did not consider the derivation of a HBGV, or application of an MOE approach appropriate for CIT, due to the lack of human dietary exposure data, the available data on genotoxicity and the uncertainties in the database. Instead, EFSA decided to characterise the risk of CIT and determine a level of no concern for nephrotoxicity in humans of 0.2 µg/kg bw per day.

72. EFSA concluded that a concern for genotoxicity and carcinogenicity cannot be excluded at the level of no concern for nephrotoxicity. Limited data on genotoxicity and carcinogenicity has been published since the EFSA evaluation, with the in vitro data supporting EFSA’s concerns over potential genotoxicity. The new in vivo data does not provide evidence for genotoxicity, but there was some indication that CIT promoted cell cycle progression at 40 mg/kg bw in rats.

73. Mean and 97.5th percentile total estimated exposures for CIT were 0-17 and 0- 43 ng/kg bw respectively and are below the level of no concern for nephrotoxicity set by EFSA. Hence, the estimated exposures are not of toxicological concern for nephrotoxicity, but carcinogenicity and genotoxicity

cannot be excluded.

74. EFSA did not derive a level of no concern for reproductive or developmental effects. While the data provided evidence for reproductive toxicity, teratogenic and embryotoxic effects of CIT at doses of 1-35 mg/kg bw maternal toxicity, including nephrotoxicity, was also reported. Hence, the reproductive and developmental effects might be secondary to maternal toxicity. A separate study failed to determine the amount of CIT that would cross the placenta, but no metabolites of CIT were detected in the foetus. The doses administered in the available reproductive and development studies were higher than the level of no concern for nephrotoxicity.

75. Studies published since EFSA's evaluation support their conclusion on development and reproductive toxicity, with toxic effects reported in the offspring and dams including nephrotoxicity at doses of 1 mg/kg bw (in feed). Female rats dosed at 0.19-4.5 mg/kg bw (in drinking water) showed adverse effects (LOAEL) at 2.25 mg/kg bw for toxicity in the kidneys, liver, and female genital organs/tracts. (Please note this study was not carried out on pregnant rats).

76. Estimated exposures for CIT in this assessment are also below any doses applied in developmental or reproductive animal studies.

77. The current assessment was based on consumption data from the NDNS for women of maternal/childbearing age and therefore may not be representative of maternal diet. In addition, the NHS recommends that those who are pregnant or planning to become pregnant should not drink alcohol. The inclusion of the UB values for wine, beer, alcopops and cocktails in the assessment may therefore lead to an over estimation of exposure when considering pregnant women.

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