5.29 PICOXYSTROBIN (258)

TOXICOLOGY

Picoxystrobin was evaluated by JMPR in 2012, when an ADI of 0–0.09 mg/kg bw and an ARfD of 0.09 mg/kg bw were established. However, the Meeting was unable to conclude on the toxicological relevance of estimated intakes of picoxystrobin metabolite IN-H8612 due to equivocal data in an in vitro assay for chromosomal aberrations. The Meeting was also unable to conclude on the toxicological relevance of estimated intakes of 2-(2-formylphenyl)-2-oxoacetic acid due to a lack of toxicological studies and a structural alert identified for genotoxicity.

During the 2013 JMPR, a new in vivo mouse micronucleus study[1] for IN H8612 was submitted. The protocol used for this study is consistent with international guidelines (Organisation for Economic Co-operation and Development Test Guideline No. 474). This in vivo study was evaluated by the Meeting and showed no evidence of genotoxicity. This allayed the concern from the in vitro study evaluated previously.

Conservative estimates of exposure were 0.2 µg/kg bw per day for chronic exposure and 0.6 µg/kg bw for acute exposure. Both estimates of exposure were below the threshold of toxicological concern for compounds with no evidence of genotoxicity (for Cramer class III, 1.5 µg/kg bw per day for chronic exposure; 5 µg/kg bw for acute exposure). The Meeting concluded that there is no concern for dietary exposure to IN-H8612.

No new data were submitted for 2-(2-formylphenyl)-2-oxoacetic acid. The company informed the Meeting that it was unable to synthesize the compound in sufficient amounts to perform an in vivo mouse micronucleus study, but that residues in soya beans were expected to be exceedingly low and therefore dietary exposure would be expected to be insignificant. The Meeting concluded that additional genotoxicity testing (e.g., an Ames test) and/or information on residues would be required in order to facilitate the further evaluation of this metabolite.

An addendum to the toxicological monograph was not prepared.

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[1] Myhre A (2013). IN-H8612: Mouse bone marrow micronucleus test. Performed by DuPont Haskell Global Centers for Health and Environmental Sciences, Newark, Delaware, USA. DuPont Project No. 36929. Submitted to WHO by E.I. DuPont de Nemours, Wilmington, Delaware, USA.