

# **Exhibit 18**



Food and Agriculture  
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PRODUCTION  
AND PROTECTION  
PAPER

**227**

# Pesticide residues in food 2016

Special Session of the  
Joint FAO/WHO Meeting  
on Pesticide Residues

# REPORT 2016



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## Joint FAO/WHO Meeting on Pesticide Residues

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Report of the special session of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues Geneva, Switzerland, 9–13 May 2016

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T, toxicological evaluation

\*\* Evaluated following the recommendation of an electronic task force of the WHO Core Assessment Group on Pesticide Residues that the compound be re-evaluated due to public health concerns identified by IARC and the availability of a significant number of new studies

diazinon use, but confidence intervals were wide, reflecting uncertainty in the risk estimates, and chance could not be excluded as an explanation for the findings. Overall, there was no convincing evidence of a positive association between NHL and exposure to diazinon.

A significantly increased risk of leukaemia in the highest exposure category (> 38.8 lifetime days of diazinon exposure; RR = 3.36; 95% CI = 1.08–10.49) and a significant exposure–response relationship were observed in the AHS. Findings for intensity-weighted lifetime exposure days demonstrated a similar pattern, but did not reach significance. Two other studies reported non-significantly elevated risks of leukaemia for high versus low diazinon use and ever versus never use of diazinon, with a non-significant dose–response relationship observed using days of use per year. Overall, there is weak evidence of a positive association between leukaemia and exposure to diazinon from the AHS only. It is noted that the number of diazinon-exposed cases was low or not reported in all three available studies.

A significant 60% excess risk of lung cancer in the highest exposure category (> 38.8 lifetime days of diazinon exposure) and a significant trend across exposure categories were observed in the AHS. Findings for intensity-weighted lifetime exposure days demonstrated a similar pattern, but did not reach significance. A separate analysis of ever use of diazinon versus never use from the AHS found no evidence of elevated risk of lung cancer among spouses of farmers/pesticide applicators; however, there were only 15 exposed cases. One other study reported a non-significant elevated risk of lung cancer for ever versus never use of diazinon (based on 17 exposed cases). Overall, there is weak evidence of a positive association between lung cancer and exposure to diazinon from the AHS cohort study only.

In view of the lack of genotoxicity and the absence of carcinogenicity in mice and rats and considering the available epidemiological data from occupational exposure, the Meeting concluded that diazinon is unlikely to pose a carcinogenic risk to humans via exposure from the diet.

The Meeting concluded that the existing database on diazinon was adequate to characterize the potential hazards to the general population, including fetuses, infants and children.

### **Toxicological evaluation**

The Meeting identified inhibition of acetylcholinesterase activity as the most sensitive end-point after single or repeated doses of diazinon in all species. After considering all previously evaluated data and the new studies, the Meeting established an ADI of 0–0.003 mg/kg bw, based on the overall NOAEL of 0.3 mg/kg bw per day from all repeated-dose toxicity studies, and using a safety factor of 100. This ADI was supported by the NOAEL of 0.03 mg/kg bw per day, the highest dose tested, identified in repeated-dose studies that involved a limited number of male volunteers, with application of a safety factor of 10.

In 2006, the Meeting established an ADI of 0–0.005 mg/kg bw, based on the highest NOAEL of 0.5 mg/kg bw per day for inhibition of erythrocyte acetylcholinesterase activity at 1 mg/kg bw per day in a 92-day repeated-dose toxicity study in rats and using a safety factor of 100. In this study, the dietary concentrations of diazinon were converted to units of milligrams per kilogram body weight per day using a default conversion factor; the present Meeting considers this less reliable than the conversion using feed consumption data.

The Meeting reaffirmed the ARfD of 0.03 mg/kg bw established by the 2006 JMPR. This ARfD was based on the NOAEL of 2.5 mg/kg bw identified in studies of acute (neuro)toxicity in rats, and using a safety factor of 100. This ARfD was supported by the NOAEL of 0.21 mg/kg bw, the highest dose tested, identified in the study in which a limited number of male volunteers were given a single dose of diazinon, with application of a safety factor of 10.