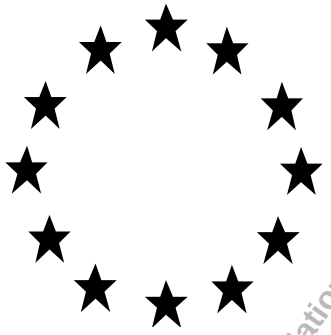
European Commission

Peer Review Programme



Paraquat

Volume 3

Annex B

ADDENDUM

to the Draft Assessment Report and Proposed Decision of the United Kingdom prepared in the context of the possible inclusion of the above active substance in Annex I of Council Directive 91/414/EEC

Summary, Scientific Evaluation and Assessment

18 NOVEMBER 2002

CONTENTS

B.5. TOXICOLOGICAL AND METABOLISM STUDIES

B 5.10.5 Acute Reference Dose (ARfD)

Paraquat can produce lung and kidney lesions in humans exposed to single exposures an acute reference dose is thus appropriate.

The dog is the most sensitive animal species and there no evidence that the dog is not a reliable model for humans.

There are no single dose studies in the available database therefore a repeat dose study has to be use. A recently submitted 6 week study in dogs had small group sizes (n=3) and showed effects at 0.75 mg/kg bw/d using capsule dosing, but lesser / marginal effects at a dose equivalent to 1 mg/kg bw/d in the diet (35 ppm). Interpretation is made more difficult by the absence of concurrent controls.

The 90 day dog study used as the basis of the short term systemic AOEL has a NOAEL of 0.55 mg/kg bw/d (20 ppm). The 1 year dog study has a NOAEL of 0.45 mg/kg bw/d. Effect levels in all these studies were $\leq$3 fold the NOAELs.

Developmental toxicity studies have NOAELs greater than the NOAELs in the dog studies.

Based on the available data it is proposed that the ARfD is set at 0.005 mg/kg bw based on the NOAEL in the 90 day dog study and a 100 fold assessment factor. It is noted that this value is possibly conservative.