



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

AUG 13 1992

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

SUBJECT: 041701. Fonofos. Response to Registrant Comments on Review of Acute and Subchronic Neurotoxicity Testing Protocols.

Tox. Chem. No. 454B
Project No. D179578

TO: Joanne Edwards, PM Team # 73
Special Review and
Reregistration Division (H7508W)

FROM: Pamela M. Hurley, Toxicologist
Section I, Toxicology Branch I
Health Effects Division (H7509C)

Pamela M. Hurley 8/7/92

THRU: Roger L. Gardner, Section Head
Section I, Toxicology Branch I
Health Effects Division (H7509C)

Roger L. Gardner
8/7/92

K/B
8/10/92

Submission: S420010

Background and Request:

In response to a Data Call-In Notice on Fonofos dated 11/18/91, ICI Americas Inc. submitted a proposed protocol for the neurotoxicity screening battery, acute and subchronic studies in rats (DP Barcode D174998). The Toxicology Branch (TB-I) reviewed and commented on the submitted protocols (for details, see memorandum from P. Hurley to J. Edwards, dated 4/16/92). The Registrant has responded to TB-I's review and TB-I has been asked to review their response.

Toxicology Branch Response:

TB-I has reviewed the submitted comments on our response to the Registrant's submitted protocols. For the most part, the Registrant has noted our comments and agrees with them. The only response from the Registrant which differs from TB-I's suggestions concerns our comment on the neuropathology examinations. TB-I's comment stated the following: "For the neuropathology examinations, it is suggested that a section from the mid-thoracic region of the spinal cord be examined as well." The Registrant responded with the following statement: "The Agency's suggestion has been noted and discussed with our

neuropathologist. ICI submits that the detection of a peripheral neuropathy which manifests itself as nerve fiber degeneration in the peripheral nerves or long fiber tracts of the spinal cord is easily and readily detected by examination of representative peripheral nerve and cervical and lumbar regions of the spinal cord. These measures have been shown to successfully detect peripheral neuropathies of the "dying back" type." TB-I accepts ICI's response to our suggestion.

TB-I notes that ICI will be submitting comments on our review of the 90-day hen study under separate cover. The Registrant will be submitting detailed comments concerning the usefulness of conducting an acute delayed neurotoxicity study when a 90-day neurotoxicity study in the hen has already been reviewed by the Agency.