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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM MAY 2 1983

TO: William Miller (16)
Insecticide Branch
Registration Division (TS-767)

THRU: William Burnam, Chief WAB
Toxicology Branch/HED (TS-769)

SUBJECT: Dimethoate Registration Standard; Registrant Correspondence re Spindle Effects Mutagenicity Testing Requirements

Attached is a suggested reply to the inquiry from Ms. Lynn Gregory in behalf of the Dimethoate Task Force.

Roland A. Gessert

Roland A. Gessert, D.V.M.
Veterinary Medical Officer
Toxicology Branch/HED (TS-769)

Attachment

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WASHINGTON, D.C. 20460

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Ms. Lynne M. Gregory
Registration Coordinator
Plant Industry Registrations
American Cyanamid Company
P.O. Box 400
Princeton, New Jersey 08540

Dear Ms. Gregory:

This is in reply to your letter of February 28, 1983 to Dr. Geraldine Werdig which you write in behalf of the Dimethoate Task Force. You ask that the assessment for spindle effects be deferred since such a test for assessment is not yet standarized.

The burden of demonstrating safety of a pesticide always has been the responsibility of those who manufacture or market the chemical. This includes developing methods to be used in demonstrating safety, especially when such methods may not yet be standarized. Therefore, we believe assessment of spindle effects should not be deferred further, but that efforts should be made to assess and interpret any spindle effects that may occur.

In a meeting with George Leber and Jon Weis of the Dimethoate European Task Force on March 4, 1982, it was recognized that spindle effects were seen in some prior experiments. The Task Force representatives suggested verifying this by doing a micronucleus test. We indicated that we were not very confident

in earlier experiments and that a less complex test might be adequate to confirm or deny the existance of "spindle effects". You could use cell lines from humans or two rodent species, treat with appropriate dimethoate concentrations, and look for an antimitotic effects (a blocking of cells in metaphase) as indicated by an increase in mitotic index. You also should look for a disruption of the spindle in metaphase. The experiment should be designed so that you may obtain a dose response and a time-action relationship.

We invite you to consult with Dr. William Schneider and/or Dr. Irving Mauer of EPA's Toxicology Branch during the course of conducting these tests.

Sincerely your,

William Miller, Ph.D.