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

MEMORANDUM

DATE: March 4, 1982

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Meeting with Dimethoate European Task Force.

FROM: William R. Schneider, Ph.D.
Toxicology Branch/HED (TS-769)

TO: Caswell File

Two members of the European Task Force for the evaluation of Dimethoate (Georg Leber and Jon Weis) met with Geri Werdig SPRD; Frank Sanders RD; Bill Burnam and Bill Schneider, Tox Branch; and Ken Bailey, HED, on February 24, 1982. They asked if a spot test would suffice for the gene mutation 3c2b requirement. I replied that the data base for the spot test is small and recommended that a gene mutation study done in cells culture would suffice for now and if it were positive it would have to be further tested.

They questioned the need for a dominant lethal test. I pointed out that a dominant lethal study using an unusual protocol indicated adverse effects. These effects needed to be verified or explained. A dominant lethal test using a more standard protocol, designed to examine the reported effects, would be of value. I mentioned that if the dominant lethal/chromosomal effects were real, then we would need to determine the magnitude of any heritable effects, which might require a heritable translocation test to be performed.

Spindle effects were also seen in some prior experiments. They wanted to do a micronucleus test to verify this. I suggested that we were not sufficiently confident in the earlier experiments and that a less complex test might be adequate to confirm or deny the existance of "spindle effects". They could use cell lines from humans and two rodent species, treat with appropriate dimethoate concentrations and look for an antimitotic effect (a blocking of cells in metaphase) as indicated by an increase in mitotic index. They should also look for a disruption of the spindle in metaphase. The experiment should be designed so that they may obtain a dose response and a time-action relationship.

If a spindle problem is confirmed, we would have to look at cells in vivo for metaphase arrest. A combined experiment might be useful in which various parameters of the same animals were examined i.e., bone marrow cells for a micronucleus study, metaphase preparations for direct spindle observation and Ames test body fluid analysis to determine relative activity throughout the treatment/post treatment period.

If the spindle problems are present in vivo then we will have to determine if the effects could involve germinal tissue. One way to do this would be to look at rodent spermatogonia. This could be done in conjunction with a in vivo experiment as described above.

cc: Caswell File, TOX
Geri Werdig, SPRD
Frank Saunders, RD
Ed Budd, TOX
Bill Burnam, TOX

OPP:HED:TOX: W.SCHNEIDER:sb 3/3/82 X73710 #m9